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FROM THE ALLERGY DIVISION OF
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ASTHMA AND HAY FEVER

Circulatory Changes Associated With Inspiratory Positive Pressure Treatment. Feinsilver, O.: Dis. Chest. **34**: 87, 1958.

Circulatory changes induced by inspiratory positive pressure treatment (IPPB) were studied in 9 patients with pulmonary disease. Three of the patients had unresolved pneumonia, 2 had asthma, and 4 had pulmonary emphysema (complicated in 2 by cor pulmonale). Emerson and Bennett equipment provided inspiratory positive pressure varying from +5 to +18 cm. of water. With a BLB mask, 100 per cent oxygen was inhaled during the procedure in which a basal dye dilution curve (Evans blue dye) was obtained and again during the administration of IPPB. The injection of dye was carried out as closely as possible at exactly 5 minutes from the time of onset of IPPB. The equipment used was the single-scale ear oximeter developed by Earl Wood. In every case there was a drop in pulse pressure due to lowering of the systolic level and variable changes in the diastolic level. The blood pressure and pulse disappeared in one case after 8 minutes of IPPB. Dilution curves showed marked alterations in all recognizable features when compared with previous curves obtained while the patients were inhaling 100 per cent oxygen. There was a uniform delay in appearance time, passage time, and maximum concentration time in every case, with prolongation of build-up time and disappearance time in most cases studied. The proportion of the curve returning to the base line showed a steplike appearance suggesting intermittent dilution of the bolus of dye by successive streams of blood entering the circulation in place of the smooth return ordinarily noted. It was concluded that a profound disturbance in the intrathoracic circulation resulted from this treatment. It was suggested that this form of treatment should be employed only when there were clear-cut indications for it and under continuous close observation of the patient. E. W.

Fractionation of Short Ragweed Pollen Extracts on Diethylaminocellulose. Robbins, K. C., Hecht, R. A., Taub, S. J., and Shields, J.: J. Immunol. **82**: 477, 1959.

Short ragweed pollen extract was fractionated under conditions of constant ionic strength and pH by gravity passage through a column of diethylaminocellulose. Three milliliter portions were collected in an automatic fraction collector, and the protein content of each portion was determined by optical density measurement. Seven fractions, each consisting of several subfractions, were isolated.

Twenty ragweed-sensitive hay fever patients were skin-tested with each of the 7 fractions and with whole pollen extract. Eighteen of the 20 patients reacted to fraction III, and 9 reacted to fractions I, V, and VI. These were considered to be the major allergens. There were few positive reactions to fractions II, IV, and VII, and these were therefore considered to be the minor allergens. All of the patients reacted to whole pollen extract. The authors believe that cellulose column fractionation is an effective means of pollen antigen separation and purification. D. Stein.

ANAPHYLAXIS

Anaphylaxis in the Mouse Produced With Soluble Complexes of Antigen and Antibody. Tokuda, S., and Weiser, R. S.: Proc. Soc. Exper. Biol. & Med. **98**: 557, 1958.

Soluble complexes of bovine serum albumin (BSA) and anti-BSA, in various regions of antigen (Ag) excess ranging from values of 8 to 180 "equivalent doses" of Ag, were prepared by adding heat-inactivated anti-BSA rabbit

serum to solutions of BSA in phosphate-buffered saline (PBS). An "equivalent dose" of Ag is that amount of Ag present in a precipitate at equivalence for any given amount of antibody (Ab). The mixtures were incubated at 37° C. for 20 minutes and then centrifuged. Challenge and control preparations were injected into the tail veins of mice previously arranged in groups according to age, weight, and sex.

Soluble BSA and anti-BSA complexes formed in the regions of 60× and 180× Ag excess produced a significantly lower mortality than was observed with complexes formed in the regions of 8×, 20×, and 40× Ag excess. Despite the questionable significance of differences observed regarding the extent of shock, the only survivors with mild shock were in the groups that received complexes formed in the regions of 60× and 180× Ag excess. Complexes converted to 180× Ag excess, after originally having been permitted to form at 8×, produced reactions comparable to those initially allowed to form at 180× Ag excess. An intravenous injection of 200 equivalent doses of Ag five minutes prior to challenge with complex formed in 8× Ag excess afforded no protection against shock. Soluble Ag-Ab complexes were also prepared by adding a concentrated solution of Ag, containing 20 equivalent doses, to precipitates formed in the zone of equivalence. Mixtures were incubated for one hour at 45° C. and then centrifuged. To one-half the supernate was added concentrated Ag to give a final solution of 180 equivalent doses of Ag. An equal volume of PBS was added to the 20× Ag solution, and both solutions of complexes were incubated at 45° C. for one hour. In marked contrast to the first experiment, the complexes in both mixtures were essentially equivalent in their anaphylactogenicity. Tests using unheated sera or physiologic saline instead of PBS in the mixtures gave anaphylactic reactions similar to the original mixtures. The nature of complexes formed in the regions of Ag excess appear to differ from those derived from solution of precipitate formed in the equivalence zone.

"Soluble BSA anti-BSA complexes formed in the regions of extreme antigen excess are less anaphylactogenic for the mouse than similar complexes formed in regions of low antigen excess. The hypothesis is advanced that anaphylactogenic activity of these complexes for the mouse is dependent upon their capacity to react with complement." H. S.

Electrical and Mechanical Responses of Uterine Smooth Muscle During Anaphylaxis In Vitro. Katsh, S., and Marshall, J. N.: Am. J. Physiol. **196**: 39, 1959.

An electronic intracellular recording apparatus was employed to study the bioelectric events which take place within smooth muscles during anaphylactically induced contraction.

Ileal segments and uterine horns of 40 sensitized female guinea pigs were studied by the ordinary Schultz-Dale technique and by the electronic recording apparatus devised for this experiment.

The Schultz-Dale technique demonstrated a high degree of sensitization in the animals and showed definite evidence of desensitization in the tissues after exposure to specific antigen.

By the use of the electronic apparatus, it was demonstrated that the resting potential diminished and action potentials were discharged just prior to the development of muscle contractions. Action potentials appeared only prior to and during the contraction of muscle, and none could be detected

during muscle relaxation. Recordings were made of the amplitude and duration of contraction as well as the rate of action potential discharge. When sensitized uterine strips were exposed to specific antigen, there was a lowering of resting membrane potential, a definite increase in the length and amplitude of contraction, and an increase in the rate of action potential discharge. Re-exposure of the shocked strips to antigen after an adequate rest period resulted in a markedly diminished responsiveness. After acetylcholine was added to the bath, there was an increase in action potential discharge and muscle contraction in desensitized relaxed uterine strips which previously had shown no evidence of action potentials.

This method of evaluating anaphylactic sensitivity may prove valuable in studying the exact mechanism and site of the anaphylactic reaction. H. F.

MISCELLANEOUS ALLERGIES

Eosinophilic Granuloma of the Lung. Livingston, H. J.: New England J. Med. **259**: 959, 1958.

A 21-year-old atopic woman, who had been under treatment for ragweed hay fever for 2 years, was admitted to the hospital because of intermittent cough of one year's duration. X-ray examination of her chest revealed extensive bilateral nodular parenchymal infiltration. The physical examination was normal. The blood chemistry was also normal. The white blood cell count was 13,500 with 64 per cent neutrophils, 2 per cent staff cells, 1 per cent eosinophils, 1 per cent basophils, 2 per cent monocytes, and 30 per cent lymphocytes. Sputum studies were negative for tubercle bacilli and fungi. Tuberculin tests as well as skin and complement-fixation tests for histoplasmosis, coccidioidomycosis, and blastomycosis were negative. Bronchoscopy was negative, and a biopsy specimen of a scalene lymph node taken for bacteriologic study showed hyperplasia but no growth of pathologic organisms. An exploratory thoracotomy revealed diffuse involvement of both lobes with shotty, nodular masses ranging from miliary to pea sized. These nodules were more profuse in the hilar area than toward the periphery. Cultures of the biopsied specimens failed to show any organisms or fungi. Microscopic examinations revealed a granulomatous lesion consisting of lymphocytes, plasma cells, histiocytes, and giant cells of the foreign body type. A great number of eosinophils were noted with areas of focal necrosis. The administration of prednisone brought about marked improvement in the cough, but no change in the nodularity was noted in the chest x-ray. After 3 months of prednisone therapy, crops of peculiar cutaneous lesions developed on the face and forearms. These appeared as superficial, patchy abrasions with a serosanguineous discharge that dried, crusted, and left a brownish discoloration. These lesions lasted for approximately 2 weeks, disappeared, and returned again in one month. Biopsy of one of these lesions revealed a superficial necrosis of the epidermis with a mild inflammatory reaction in the upper portion of the dermis. The inflammatory cells consisted of polymorphonuclear leukocytes and eosinophils. A bone study was negative. Pulmonary function studies revealed a moderate restrictive ventilatory defect. The patient has felt well on steroid therapy, but there have been no significant changes in the chest x-ray.

Eosinophilic granuloma, Letterer-Siwe disease, and Hand-Schüller-Christian disease have been classified by Lichtenstein under one heading as "histiocytosis X." The process may be localized or disseminated. The acute or

subacute disseminated forms were grouped as Letterer-Siwe syndrome, and the chronic or subchronic forms were classed as the clinical expression of the Schüller-Christian syndrome. The acute disseminated cases, which occurred in young children, had a serious prognosis. The chronic forms present in older children and adults had a favorable prognosis, unless there was rapid progression of the lesions. The presence of pulmonary lesions indicated a disseminated form of the disease. Although the etiology of pulmonary eosinophilic granuloma is unknown, hypersensitivity was favored as the most logical mechanism. Pathologically, there was a suggestive allergic angiitis, which might be related to periarteritis nodosa. Tissue eosinophilia was the rule, and eosinophils were found throughout the granulomatous nodules. Auld postulated that eosinophilic granuloma of the lung might be a chronic response to a low-grade antigen, in contrast to Löffler's syndrome, which represented a more acute reaction, with larger areas of the lung responding to the stimulus at the same time. It was suggested that the allergic theory might explain the case reported herein. E. W.

Jaundice Occurring in a Patient Treated With Chlorothiazide. Drerup, A. L., Alexander, W. A., Lumb, G. D., Cummins, A. J., and Clark, G. M.: New England J. Med. **259**: 534, 1958.

A 62-year-old Negro woman with diabetes mellitus, congestive cardiac failure secondary to arteriosclerotic disease, an enlarged liver, and xanthelasma over both eyelids was being treated in the outpatient department of a large hospital. During the 6-month period before the onset of the present illness, she had received no medication other than insulin, digitalis, and mercaptomerin. Because of the poor response to this therapy and because of the presence of congestive heart failure, 500 mg. of chlorothiazide was prescribed each day in addition to digitalis and NPH insulin. Two weeks later the patient complained of marked pruritus which had started four days after the first dose of chlorothiazide. On physical examination, it was noted that she was jaundiced. Her liver was enlarged to a point 7 cm. below the right costal margin and was firm but not tender. Liver function studies indicated an obstructive type of jaundice. Repeated blood smears failed to show an eosinophilia. A needle biopsy of the liver showed focal bile staining of the liver cells with bile thrombi in the canaliculi. There was a mild degree of fibrosis with minimal round-cell infiltration around the portal tracts, but no evidence of necrosis or other abnormality of the parenchymal liver cells. Because of the unremitting jaundice, an exploratory laparotomy was performed. No extrahepatic mechanism for obstruction could be demonstrated. A wedge biopsy of the liver showed essentially the same changes as the needle biopsy. After operation, the patient underwent an uneventful convalescence with a gradual return of all liver function studies to within normal limits in two months. Six months after surgery the patient died of congestive heart failure. Aside from congestive changes, the histologic examination of the liver revealed healing irregular necrotic areas which might have been caused by some toxic agent.

Among drugs known to cause jaundice of the intrahepatic cholestatic type are arsphenamine, methyltestosterone, thiouracil, para-aminosalicylic acid, methimazole and, more frequently, chlorpromazine. A careful review of this patient's history revealed that she had taken none of these compounds. The evidence in this case suggests that the intrahepatic obstructive jaundice was produced by the chlorothiazide therapy. E. W.

Chlorpromazine-Type Cholangitis. Report of a Case Occurring After Administration of Prochlorperazine. Mechanic, R. C., and Meyers, L.: New England J. Med. **259**: 778, 1958.

A 68-year-old woman, who had taken a total of 10 capsules each containing 10 mg. of prochlorperazine and 5 mg. of isopropamide within a week, was hospitalized because of jaundice and severe generalized pruritus. Physical examination was negative except for the jaundice. The white cell count was relatively normal, with 5 per cent eosinophils. The urine was strongly positive for bile and urobilinogen. The serum alkaline phosphatase was 10.7 Bodansky units, and the serum glutamicoxalacetic transaminase was 77 units. Because of a rise in the serum alkaline phosphatase and bilirubin 10 days after admission, and because the absence of a history of ingestion of an icterogenic drug, an exploratory operation was performed. At laparotomy the liver and biliary tree were grossly normal. Liver biopsies demonstrated the hepatic architecture to be intact. There was marked bile retention, predominantly in a pericentral location, involving both the bile canaliculi and the hepatic parenchymal cells. Bile pigment was also seen within the Kupffer cells in this region. The sinusoids in the pericentral location were moderately distended. Many of the typical features of a chlorpromazine type of cholangitis were present in this case. E. W.

Thrombocytopenic Purpura Associated With Sulfamethoxypyridazine Administration. Green, I., and Finkel, M.: New York J. Med. **59**: 2034, 1959.

A 64-year-old white man in acute cardiac failure and mild pyuria was given sulfamethoxypyridazine, 0.5 Gm. twice a day for 7 days and then 0.5 Gm. daily for the succeeding 5 days. On the last day of therapy the patient had an unexplained bout of hypotension, and the medication was stopped. During the succeeding 24 hours he developed a severe nosebleed and a generalized petechial rash over the entire body. The Rumpel-Leede test was markedly positive, and the platelet count was 5,000 per cubic centimeter. Bone marrow aspiration revealed a hypocellular marrow with a normal myelocyte-erythrocyte ratio and the usual number of normal megakaryocytes. The only other medications which he received consisted of Digoxin, 0.25 mg. twice daily; Nembutal, 50 mg. daily; and a single 10 mg. dose of Compazine 4 days after the onset of the rash. Within 2 weeks following the cessation of the medication his platelet count gradually returned to normal, the rash cleared, and the Rumpel-Leede test rapidly became negative. At this time in vitro studies using the technique of Ackroyd were performed. When the patient's platelet-rich citrated plasma was mixed with a saturated solution of sulfamethoxypyridazine, no clumping or agglutination of platelets was noted. Since sulfamethoxypyridazine is retained in the blood stream for long periods of time at a high level, the author suggests that this characteristic of the drug may potentiate its sensitizing properties. R. W.

Agranulocytosis Following Acetazoleamide Therapy. Arora, Y. C.: New York J. Med. **59**: 119, 1959.

A 50-year-old white housewife was admitted to the hospital because of fatigue and a tendency to bruise easily. These complaints were of approximately 3 weeks duration. She had been receiving treatment for rheumatoid arthritis with 15 mg. of prednisone daily for 2 years. Recently triamcinolone had been used in place of prednisone. During the past 6 months she had also received 250 mg. of acetazoleamide daily for relief of ankle edema. Two weeks prior to admission, following several days of symptoms, her white cell

count was 2,200 with 21 per cent granulocytes. Just prior to admission the leukocyte count had dropped to 1,550 with 16 per cent granulocytes. None of the counts showed evidence of anemia. The physical examination on admission to the hospital was essentially negative except for a slight elevation of temperature and a few ecchymotic and petechial areas on both lower extremities. The hemoglobin, red cell count, and platelet count were all normal, while her total white count was 1,900 with a differential of 7 per cent lymphocytes, 5 per cent monocytes, 12 per cent stab forms, 11 per cent segmented cells, and 23 per cent total granulocytes. Blood chemistries and clotting studies were normal, and bone marrow examination showed normal total cellularity with somewhat more numerous granulocyte cells. There was an increase above normal in the myeloid erythroid ratio. The myelocytes were also increased, whereas the number of mature segmented cells in the marrow was substantially reduced. The marrow suggested a disturbance in the maturation response at the metamyelocyte level, along with a degenerative process which had affected the granulocyte series. The patient was placed on Achromycin and maintained on triamcinolone, 4 mg. twice daily, and all other medication was stopped. The patient made an uneventful recovery during the ensuing 3 weeks. R. W.

Protective Measures Against Stinging Insects. Morse, R. A., and Ghent, R. L.: New York J. Med. **59**: 1456, 1959.

Patients who are hypersensitive to the bites of stinging insects are advised to observe certain precautions when in the vicinity where these insects may be present. Light-colored clothing made of a smooth fabric, such as cotton, nylon, or khaki, should be worn, rather than rough-textured, dark-colored clothing, such as tweeds, woolens, or flannels. Members of the Hymenoptera family are particularly attracted by the odor of leather or suede products; hence, these materials should be avoided. Women are advised to wear scarves over their hair so that the insect will not become enmeshed. Perfumes or other types of scented cosmetics should not be used, since these odors attract insects. Since bees are more likely to bite a moving object, it is best to move very slowly when near them in order not to attract them. Covering the eyes with the hands and moving very slowly away from the insect is the best maneuver. Only if a swarm of insects is encountered should rapid escape be attempted. Following a sting by a honeybee, the stinger and venom sac should be removed as quickly as possible by scraping the skin. Speed in carrying out this maneuver will markedly lessen the severity of the reaction. Bees rarely fly when the temperature is below 60° F. and are therefore less likely to be encountered on a cool day. R. W.

Rice Intolerance in Infants: Masked Food Allergy? Johnstone, D. E.: Ann. Allergy **17**: 350, 1959.

In infants, intolerance to rice frequently causes increased hunger, colic, diarrhea, rhinorrhea, cough, and wheezing.

Rice intolerance was noted in 22 of 157 (14 per cent) infants with a positive family history for major allergic disease; however, only 2 of 75 (2.6 per cent) infants with negative family history of allergy were intolerant to rice.

Of 28 infants with major allergies, 14 per cent had symptoms of rice intolerance. Out of a group of 24 infants with symptoms of rice intolerance, positive skin reactions were elicited to rice in 2, to oats in 1, to wheat in 4, and to milk in 3. Skin tests performed in 15 normal infants with a negative family

history of allergy resulted in 1 positive reaction to rice and 1 to wheat. Eight of the infants with rice intolerance subsequently developed major respiratory allergies within 3 years. H. F.

Agranulocytosis Following Administration of Phenothiazine Derivatives. Piciotta, A. V., Ebbe, S., Lennon, E. J., Metzger, G. O., and Madison, F. W.: Am. J. Med. **25**: 210, 1958.

Agranulocytosis was observed in 16 patients treated with chlorpromazine. The total dosage of chlorpromazine administered before the appearance of granulocytopenia ranged between 2 Gm. and 112 Gm., and the number of days of treatment varied from 10 to 401. In 50 per cent of the cases, agranulocytosis was suspected after the onset of symptoms of infection, principally of the respiratory tract but also cellulitis, proctitis, or bacteremia. In the remainder of the cases, agranulocytosis was discovered on routine blood counts. None of the patients manifested any allergic symptoms. When agranulocytosis developed, there was a precipitous decrease of the leukocyte count, which reached its lowest level 2 to 5 days after the decrease had begun. The erythrocytes, platelets, and reticulocytes were normal in number. The total number of white cells at the lowest point varied between 200 and 3,500 per cubic millimeter. At the height of leukopenia, the bone marrow showed a selective aplasia of cells of the granulocytic series but no involvement of erythropoietic or thrombopoietic centers. During recovery, progranulocytes made their appearance and, as recovery progressed, myelocytes were seen. When complete recovery occurred maturation extended to the metamyelocytes, and band forms were seen. With discontinuance of the drug, granulopoiesis was resumed 5 to 10 days. There was no clinical evidence of peripheral destruction of leukocytes. Extensive immunologic studies were performed. The sera of the patients were mixed with varying quantities of chlorpromazine and a suspension of leukocytes obtained from a compatible donor or from the patient following recovery. These systems were observed grossly and by phase contrast microscopy for leukagglutination. In no instance did leukagglutination occur. Leukolysins were sought by incorporating complement with the serum-chlorpromazine-white cell mixtures and by performing serial leukocyte counts at intervals. There was no significant diminution in the number of leukocytes and, therefore, no in vitro evidence of white cell lysis. In one case, chlorpromazine was readministered in lower dosage for one year without recurrence of the untoward hematologic reaction. In another case, granulocytopenia followed therapy with a cumulative dose of 18.5 Gm. of chlorpromazine given over 121 days. One year following recovery, promazine was given. Agranulocytosis again developed in 21 days, during which time the patient had received 5.025 Gm. One year later, agranulocytosis again developed for a third time following the administration of 13.7 Gm. of prochlorperazine over a period of 44 days. In all of these instances the reaction was delayed. It was concluded that agranulocytosis produced by phenothiazine derivatives is not predicated on an allergic basis. E. W.

PHARMACOLOGY, PHYSIOLOGY, AND PATHOLOGY

Abnormal Sweat Electrolytes in Patients With Allergies. A Preliminary Report. Hsia, D. Y., Driscoll, S. G., Greenberg, D., Lee, T. C., and Lanoff, G.: A. M. A. J. Dis. Child. **96**: 685, 1958.

The sweating mechanism of 123 allergic patients was studied. In order to stimulate sweating, infants were placed inside plastic bags and older patients

were wrapped in blankets and simultaneously had heat applied externally with a heating pad. Palmar sweat chlorides were estimated by the agar plate method described by Shwachman and Gahm. The hands were first washed, rinsed, and dried before sweat stimulation was begun. An imprint of the hand or fingers was made on the agar surface 20 minutes later, so that the amount of sweat chlorides which accumulated during the test period could be measured. The amount of sweat elaborated by each patient was graded as 1, 2, 3, or 4 plus, depending upon whether more or less than 25 mEq./L., 75 mEq./L., or 150 mEq./L. was obtained. Only 3 plus or 4 plus reactions were regarded as indicative of significantly increased sweating. Sixty-eight of the 123 allergic patients (56 per cent) developed positive reactions, whereas only 128 of 1,001 persons (13 per cent) in the control group showed positive responses. Similar results were obtained in patients of both the younger and older age groups. Such factors as sex and race did not seem to influence the sweating mechanism. Since patients with cystic fibrosis are known to excrete excessive quantities of both sodium and chloride in their sweat, the authors sent out questionnaires to families with allergic disease to determine whether there was an increased incidence of cystic fibrosis among allergic families. The data obtained were essentially negative. Sweat plate studies carried out among patients with chronic respiratory disease or emphysema showed that these persons had no increased sweat excretion. R. W.

Cardiovascular Effects of Sympathomimetic Bronchodilators: Epinephrine, Ephedrine, Pseudoephedrine, Isoproterenol, Methoxyphenamine and Isoprophenamine. Aviado, D. M., Jr., Wnuck, A. L., and de Beer, E. J.: J. Pharmacol. & Exper. Therap. **122**: 406, 1958.

Six bronchodilator drugs were administerd directly into the arterial supply of the bronchi, legs, splanchnic areas, and heads of anesthetized dogs. The lungs were artificially ventilated at a constant pressure. All of the drugs caused vasodilation. On a milligram-for-milligram basis, the injection of isoproterenol into a bronchial artery was twice as effective as the injection of epinephrine. Isoproterenol and epinephrine were effective in 10 and 20 *microgram* doses, respectively. The threshold effective dose for pseudoephedrine was 5 mg., and for ephedrine, methoxyphenamine, and isoprophenamine it was 10 mg. each. Systemic effects did not occur with this technique. On intravenous injection, hypotension was noted with isoproterenol, methoxyphenamine, and isoprophenamine. The other 3 drugs were variable, producing bronchial constriction or dilatation, hypertension, and bradycardia.

Intravenous injection of epinephrine or isoproterenol increased the force of myocardial contraction. Although, on initial injection, ephedrine and pseudoephedrine increased the force of contraction, subsequent injections caused depression, usually accompanied by hypotension and lessened pulmonary venous outflow. Methoxyphenamine and isoprophenamine consistently reduced myocardial force of contraction and caused systemic hypotension.

It was concluded that sympathomimetic bronchodilators were not selective in action and that they had significant systemic vascular effects. E. K.

Cardiovascular and Respiratory Effects of Lethal Doses of Histamine and Compound 48/80 in Rabbits. Papacostas, C. A., and Loew, E. R.: Proc. Soc. Exper. Biol. & Med. **100**: 605, 1959.

Compound 48/80 liberates sufficient amounts of histamine from the tissues to produce the features of histamine and anaphylactic shock in some species.

In the rabbit, however, lethal doses of histamine and compound 48/80 produce death by different mechanisms. Lethal doses of the histamine liberator produced pronounced depression of the respiratory system in anesthetized rabbits. The animals could be kept alive by artificial respiration, and blood pressure and electrocardiographic readings taken at this time showed no serious effects of the drug on the cardiovascular system. Lethal doses of histamine, under similar experimental conditions, produced a rapid and marked fall in blood pressure with severe changes in the electrocardiographic recordings. The entire cardiovascular system appeared to be involved, and artificial respiration could not save these animals. Hence, toxic doses of histamine and compound 48/80 produce death in the rabbit by affecting different systems. Under these experimental conditions, compound 48/80 did not liberate enough histamine to elicit the symptoms of histamine shock. B. S.

IMMUNOLOGY

Delayed Hypersensitivity In Vitro. III. Effect of Cortisone on Cytotoxicity of Mumps Viral Antigen. Glasgow, L. A., Sanchis-Bayarri, V., and Morgan, H. R.: Proc. Soc. Exper. Biol. & Med. **98**: 614, 1958.

Guinea pigs were infected with an egg-adapted strain of mumps virus by both ocular and nasal routes. Three to four weeks after infection, the guinea pigs were skin tested with mumps virus antigen. The animals were then sacrificed and the spleens were removed under sterile conditions. Fragments of splenic tissue were placed on a rooster plasma coagulum in T-9 flasks, and 2 ml. of a special medium was added to each. Cortisone acetate, 25 gamma/ml., was introduced into the medium prior to placing it in the flasks approximately 24 hours before the addition of mumps virus antigen. Positive intracutaneous reactions, characterized by areas of induration from 3 to 10 mm. in diameter, developed in 15 of the 21 inoculated guinea pigs. None of the control animals developed positive skin tests.

Previous observations on the *in vitro* cytotoxic reaction between mumps virus antigen and hypersensitive cells were confirmed. Inhibition of the migration of macrophages was marked for those fragments exposed to mumps virus antigen. The cells also showed evidence of progressive destruction, as compared with the controls. The addition of cortisone to the medium prior to introduction of the antigen partially protected the fragments from the cytotoxic action of viral antigen, both quantitatively and qualitatively. Mild toxic effects were noted, but these were slight in comparison to the controls. The similarity to previous studies with tuberculin suggests a possible relationship between hypersensitivity to mumps virus antigen and the therapeutic effectiveness of corticosteroids against the complications of mumps virus infections. H. S.

Transfer of Acquired Tolerance to Skin Homografts in Mice. Martinez, C., Smith, J. M., Aust, J. B., Mariani, T., and Good, R. A.: Proc. Soc. Exper. Biol. & Med. **98**: 640, 1958.

Previous studies have established that acquired tolerance to homotransplantation of various tissues can be induced in animals of different species by the injection at birth of living foreign spleen cells. In this study, inbred mice of two genetically nonrelated strains, ZBC and Ce, were used. Tolerance to Ce skin homografts was established in ZBC animals by treating them at birth with intravenous injections of 2 to 4 million living spleen cells taken from

adult Ce donors. At approximately 2 months of age, each treated ZBC animal received a full-thickness skin graft from an adult Ce donor. Recipients were considered tolerant if they accepted the skin graft for no less than two months. In an attempt to transfer the acquired tolerance, cell suspensions were made from the spleens of the tolerant ZBC animals and injected into newborn mice of the same strain. At 2 months of age, these recipients were tested for tolerance to Ce homografts. Untreated ZBC animals were grafted as controls.

"The incidence of successful Ce skin grafts in ZBC animals injected at birth with living spleen cells taken from Ce donors was 94 per cent of a total of 35 mice tested. Similarly the incidence of successful Ce skin grafts in ZBC animals injected at birth with living spleen cells taken from ZBC donors made previously tolerant to Ce tissues was 83 per cent from a total of 30 animals." The difference in incidence between the two groups is not statistically significant. Sixty-six nontreated ZBC controls all rejected the Ce homografts. These findings indicate that transfer of acquired tolerance to an isologous individual can be accomplished by the injection at birth of spleen cells from a tolerant donor. H. S.

Antigens of Rabbit Semen. Weil, A. J., and Finkler, A. E.: Proc. Soc. Exper. Biol. & Med. **98**: 794, 1958.

The immunologic relationship between spermatozoa and seminal plasma was studied in the rabbit. The results were compared with previous studies performed in man and in the guinea pig. Immune sera of high antibody titer were obtained in guinea pigs after two intramuscular injections at two-week intervals of 0.5 ml. of equal parts of Freund's adjuvant and either rabbit seminal plasma diluted with physiologic saline or rabbit spermatozoa washed in saline and adjusted to standard concentration. After 3 to 4 weeks the sera were collected and pooled. The reactions of antiseminal plasma and antispermatozoal sera were indistinguishable from each other in the complement fixation test against seminal plasma, spermatozoa, and fractions of spermatozoa obtained following prolonged refrigeration or sonic vibration. There was only slight cross-reactivity to extracts of testes, epididymis, prostate, kidney, and liver. No cross-reactivity with rabbit preimmunization serum was noted. No cross-reactivity with human seminal products was observed.

Antiseminal plasma and antispermatozoal sera each agglutinated tanned erythrocytes treated with seminal plasma in serum dilutions up to 1/40,000. Tanned erythrocytes on which the content of seminal vesicles had been absorbed were agglutinated by both antisera in dilutions up to 1/16,000. Tanned erythrocytes exposed to organ extracts were not agglutinated by sera in dilutions of 1/25. Both fresh semen and semen suspended in physiologic saline produced strong slide agglutination reactions with both antisera. In the Ouchterlony test, antiseminal plasma and antispermatozoal sera gave the same precipitation lines against seminal plasma.

In both man and the rabbit, seminal plasma and spermatozoa contain powerful closely related antigens which resist differentiation and are highly species- and organ-specific. The multiplicity of antigenic components, demonstrable by agar diffusion, corresponds with what has previously been described in man and the guinea pig. The view that the antigenic material does not originate with the spermatozoa is strengthened by the low degree of cross-reactivity of rabbit sera and extracts of testes and epididymis and by the evidence that extracts of seminal vesicle contain some antigenic components reactive with antiseminal plasma and antispermatozoal immune sera. Moreover,

seminal vesicle fluid contains nearly all the antigenic components demonstrable with both immune sera. It appears that the antigens of seminal plasma and spermatozoa originate in the seminal vesicle. H. S.

Immunological Unresponsiveness in Rabbits Produced by Neonatal Injection of Defined Antigens. Smith, R. T., and Bridges, R. A.: J. Exper. Med. **108**: 227, 1958.

Neonatal animals not only fail to produce antibody in response to antigenic stimulation but are rendered unresponsive to the specific antigen when they encounter it in later life. Neonatal rabbits were given a single intraperitoneal injection of bovine serum albumin (BSA), ovalbumin (EA), or human gamma globulin (HGG). Further antigenic challenges were made at 3 to 4 months of age and repeated at 4-month intervals. Diphtheria toxoid, typhoid-paratyphoid vaccine, BCG vaccine, meningococcal endotoxin, and Group A streptococcal vaccines were also used as antigens by other routes.

The minimal amount of BSA given at birth and effective in suppressing antibody response for 3 to 4 months was found to be between 10 and 20 mg. With large doses of BSA, unresponsiveness could be elicited only if the initial antigen stimulus was administered within the first 2 weeks of life. Such a dose produced unresponsiveness lasting at least 90 to 120 days. Although its duration was related to the amount of antigen given initially, the unresponsive state could be prolonged indefinitely by repeated antigenic challenge. Egg albumin antigen produced a similar picture. The minimal neonatal dose was 10 mg. More than this amount produced unresponsiveness for at least 167 but less than 262 days. Unresponsive rabbits excrete antigen at a linear rate and over a prolonged period as compared with animals which are forming antibody. Animals rendered unresponsive to BSA by a neonatal injection of BSA showed a normal immune response to EA in the challenge period. Induced unresponsiveness to antigen is specific. Oral administration of 260 mg. BSA on the day of birth resulted in detectable serum levels at 1 to 3 days of age. Many of these animals became immunologically unresponsive for from 54 to 117 days following the single exposure. Greater individual variation was found than when antigen was administered parenterally.

Lymphoid tissue cells taken from animals effectively immunized to BSA were transferred to unresponsive rabbits. The recipients could then produce antibody in normal fashion. Quantitative antibody responses indicated that no humoral inhibitor was operating in the formerly unresponsive rabbits. Any antigen persisting from the neonatal injection "was either located in sites which prevented significant binding of the antibody produced by the immune cells, or was present in amounts too small to affect the antibody levels significantly." Two months after lymphoid cell transfer and response to antigen these recipient rabbits reverted to their unresponsive state. Lymphoid cells from unresponsive rabbits transferred to normal or x-irradiated rabbits failed to show a response to antigenic stimulation. A wide spectrum of bacterial antigens injected into neonatal animals failed to induce an unresponsive state as judged by challenge at 3 months of age.

It was concluded that "the requirements for prolonged immunological tolerance include (a) initial exposure to a threshold amount of the antigen around the time of birth, and (b) a continuous source of the antigen." The persistence of antigen in a site unavailable to reaction with administered antibody seemed to be an important consideration. E. K.

Immunization With Asian-Strain Influenza Vaccine Equivalence of the Subcutaneous and Intradermal Routes. McCarroll, J. R., and Kilbourne, E. D.: New England J. Med. **259**: 618, 1958.

An unselected group of 362 hospital employees between the ages of 18 and 65 years, received Asian-strain influenza vaccine according to different schedules which varied in dosage, in timing, or in route of administration. All subjects were bled on the day of initial vaccination and 14 days following the first injection of vaccine. Serum specimens were titrated for hemagglutination-inhibiting antibody by the serum serial-dilution technique, with a relatively "insensitive" virus strain and a ferret passage line of the same virus to provide a maximally "sensitive" test for the presence of antibody.

Titration of prevaccination serums disclosed that less than 10 per cent of the subjects possessed detectable antibody. In postvaccination serums antibody was detected in 53 to 86 per cent of subjects (depending on the test method used) who received a single injection of the largest dose (1.0 ml. subcutaneously. Division of this single 1.0 ml. subcutaneous dose into two 0.5 ml. injections one week apart increased the occurrence of demonstrable antibody to from 71 to 91 per cent; a comparable response (84 to 89 per cent) was noted when vaccine was given subcutaneously in two doses of only 0.2 ml. each, one week apart. Even in the groups in which only two 0.1 ml. injections were given (subcutaneous route in one group, intracutaneous in the other) at a 7-day interval, antibody responses were induced in 44 to 84 per cent of subjects—values not greatly dissimilar to those obtained when five times the quantity of vaccine was employed in a single subcutaneous dose. When the groups receiving intracutaneous vaccine were compared with those in which the same dose of vaccine was given subcutaneously, the percentage of subjects in whom antibody developed was greater among those who received vaccine subcutaneously. It was concluded that division of vaccine into 2 injections given 7 days apart induced a response superior to that effected by the same total dose in a single injection. Small doses administered subcutaneously were at least as effective in antigenic efficiency as equivalent doses administered intracutaneously. E. W.

The Antigen of Echinococcus. Magath, T. B.: Am. J. Clin. Path. **31**: 1, 1959.

The subject of echinococcus antigen is reviewed. It is noted that, with the addition of thimerosal to echinococcus cystic fluid, the ability of this fluid to elicit wheal-flare skin reactions on testing may persist for more than 25 years. Patients tested 25 years after removal of their cysts still show positive skin tests "which probably persist throughout life." Complement-fixation tests are also used to detect echinococcus antigen, being positive in 93 per cent of a series of patients proven to have live cysts. About 87 per cent of these patients give positive skin reactions to the Casoni test. False positive reactions to complement-fixation testing are rare. Positive indirect agglutination tests have been obtained in this disease. Filter paper electrophoresis of cystic fluid followed by complement-fixation testing of the various segments shows that the antigen moves with the gamma globulin fraction. The antigen is further localized as appearing in a protein-free, acetone-ether insoluble fraction. Serum antibody for echinococcus material is also found moving with the gamma globulin fraction on paper electrophoresis. Cystic fluid is an active antigen when injected into rats, eliciting complement-fixation antibody. However, such immunization does not produce sera which show lines of precipitation on double diffusion agar plates. Sera from echinococcus-infected rats and human beings show lines of precipitation with hydatid antigen, with evidence of

cross-reaction between *E. granulosus* and *E. multilocularis*. Sera from patients with hydatid disease show no precipitin reaction when tested with alpha, beta, or gamma globulin fractions of cyst antigen, but a line of precipitation is elicited by the albumin fraction of antigen. The substance in the gamma globulin fraction of antigen gives a complement-fixation reaction but not precipitation. E. K.

The Dysgammaglobulinemic Syndrome. Hammack, W. J., Bolding, F. E., and Frommeyer, W. B.: Ann. Int. Med. **50**: 288, 1959.

Discrete and homogeneous globulin peaks in protein electrophoretic patterns were observed in 4 patients with unusual susceptibility to infection.

Immunologically, the serum proteins of 3 of the patients were related to myeloma proteins, while those of the fourth patient were related to macroglobulin. Anticomplementary activity was present in the serum of 3 of the patients. No other evidence of signs pointing to multiple myeloma was noted during the three and one-half years that these patients were under observation.

The authors believe that although there is a possibility that multiple myeloma may develop sometime in the future, these patients have a separate syndrome which they refer to as dysgammaglobulinemia. This term was coined to imply that these 4 patients have a disturbed function of the gamma globulins which is manifested by repeated infections and also that there may be multiple etiologies for this disturbance. H. F.

Production of Antibody in Patients With Uremia. Stoloff, I. L., Stout, R., Myerson, R. M., and Havens, W. P.: New England J. Med. **259**: 320, 1958.

Recently it has been reported that 4 of 9 renal homotransplants performed in patients with terminal renal failure have functioned for periods of 4 to 5½ months, a duration of viability much longer than that usually seen in man or laboratory animals. The prolonged survival of homotransplants of skin noted in another group of patients with uremia posed the question whether the state of uremia reduces the immunologic response of the hosts to the transplants. In the present study, 14 Schick-negative patients with azotemia associated with chronic glomerulonephritis, chronic pyelonephritis, obstructive uropathy, and malignant hypertension were injected with purified diphtheria toxoid, and the anamnestic response was measured. The production of antitoxin under these circumstances follows a more predictable pattern than the primary response of Schick-positive persons. As a control for the Schick test, each patient was also inoculated intracutaneously with 0.1 ml. (0.08 Lf dose) of diphtheria toxoid. The reactions were read at the end of 48 hours, and patients who had negative Schick tests and showed no allergic pseudoreactions were inoculated intramuscularly with 50 Lf doses (0.14 mg). of highly purified diphtheria toxoid. Blood was drawn 7, 14, 21, and 28 days after immunization, and the amount of diphtheria antitoxin in each serum was determined by titration in the skin of rabbits. The antibody response of patients with azotemia, with one exception, was characterized by an increase in circulating antitoxin which reached a peak usually by the fourteenth or twenty-first day and thereafter gradually declined. This pattern was qualitatively and quantitatively similar to that found in previous studies on normal persons and on persons with other conditions known not to influence the production of antibody. The evidence accumulated supported the concept that suppression of circulating antibody has little to do with the enhanced survival of renal homografts in uremic patients. E. W.

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Hollywood Beach Hotel, Hollywood-by-the-Sea, Florida
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VOL. 30, NO. 6 NOVEMBER—DECEMBER, 1959

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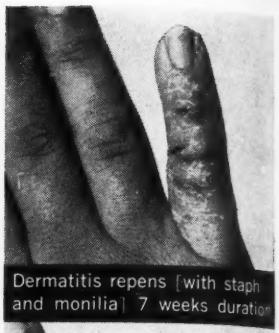

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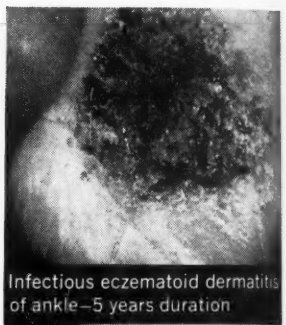

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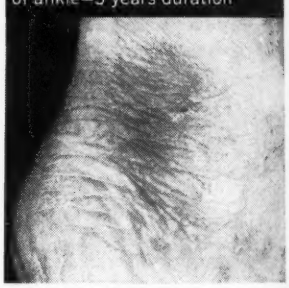

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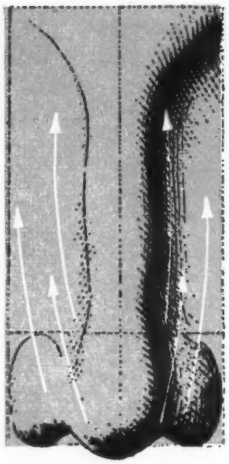

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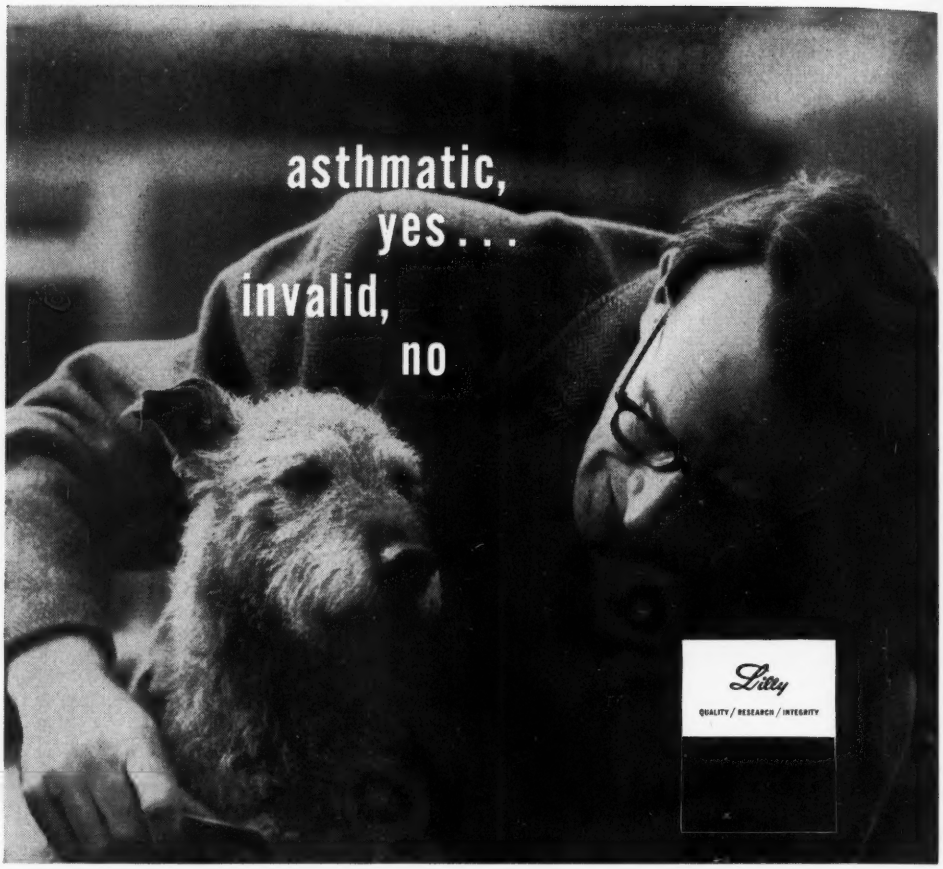

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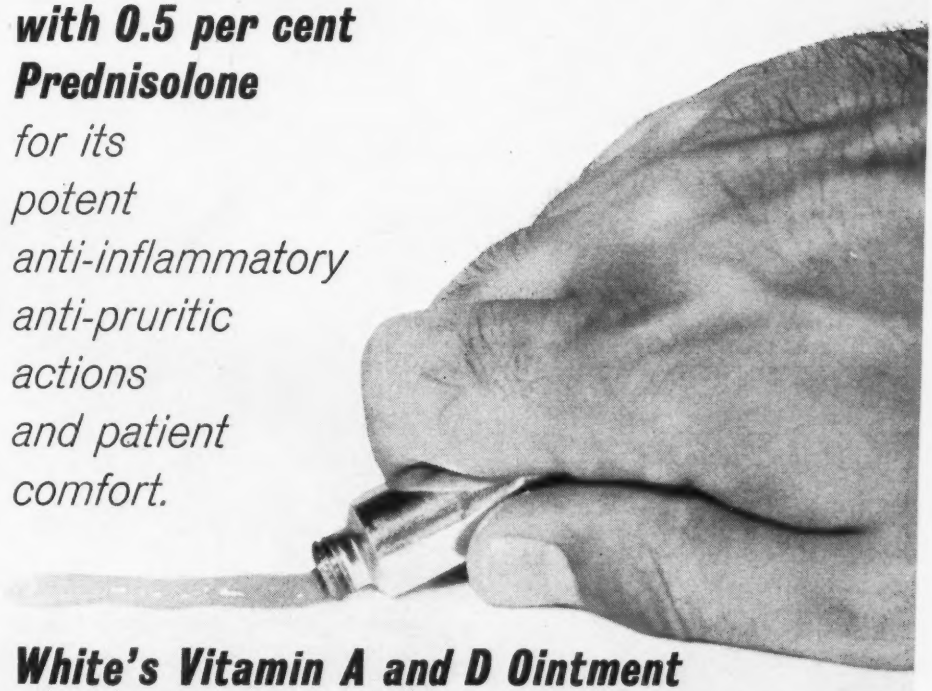

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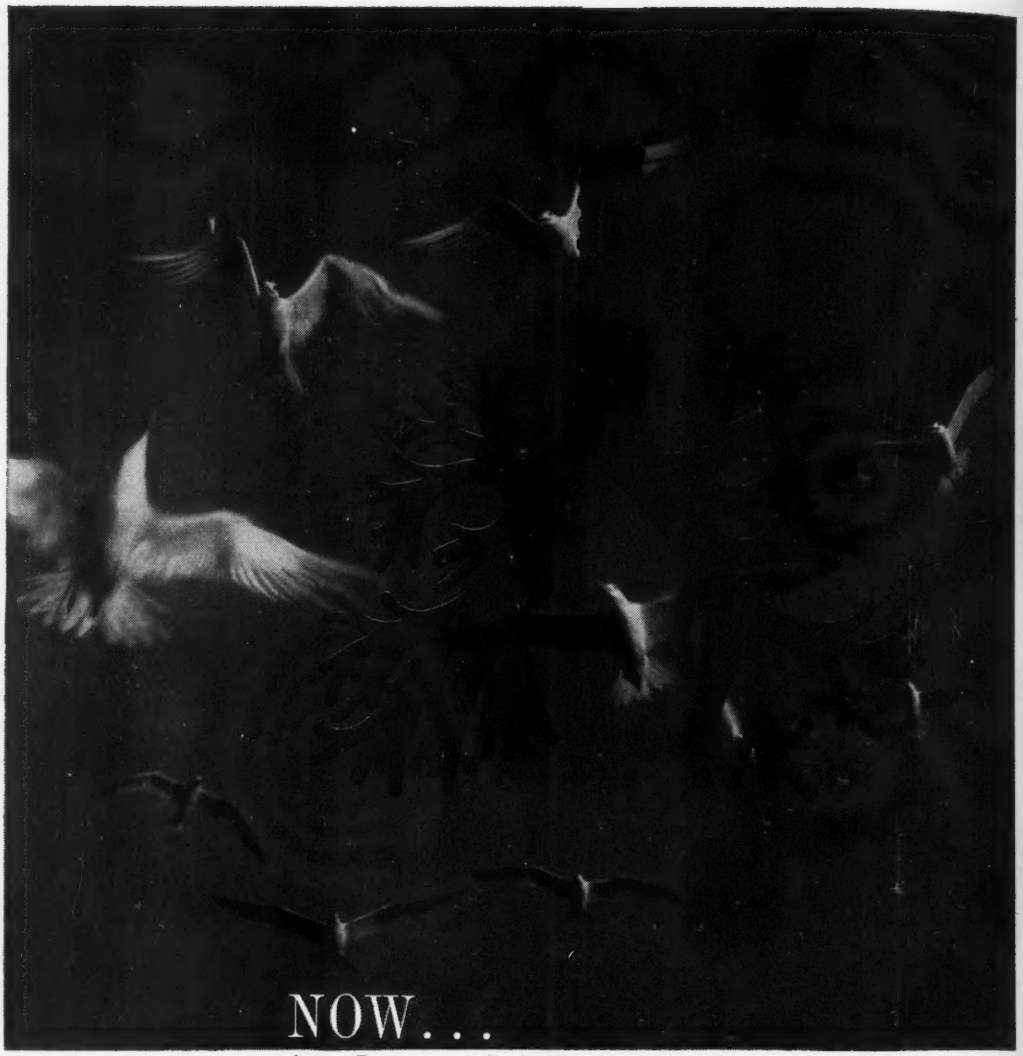

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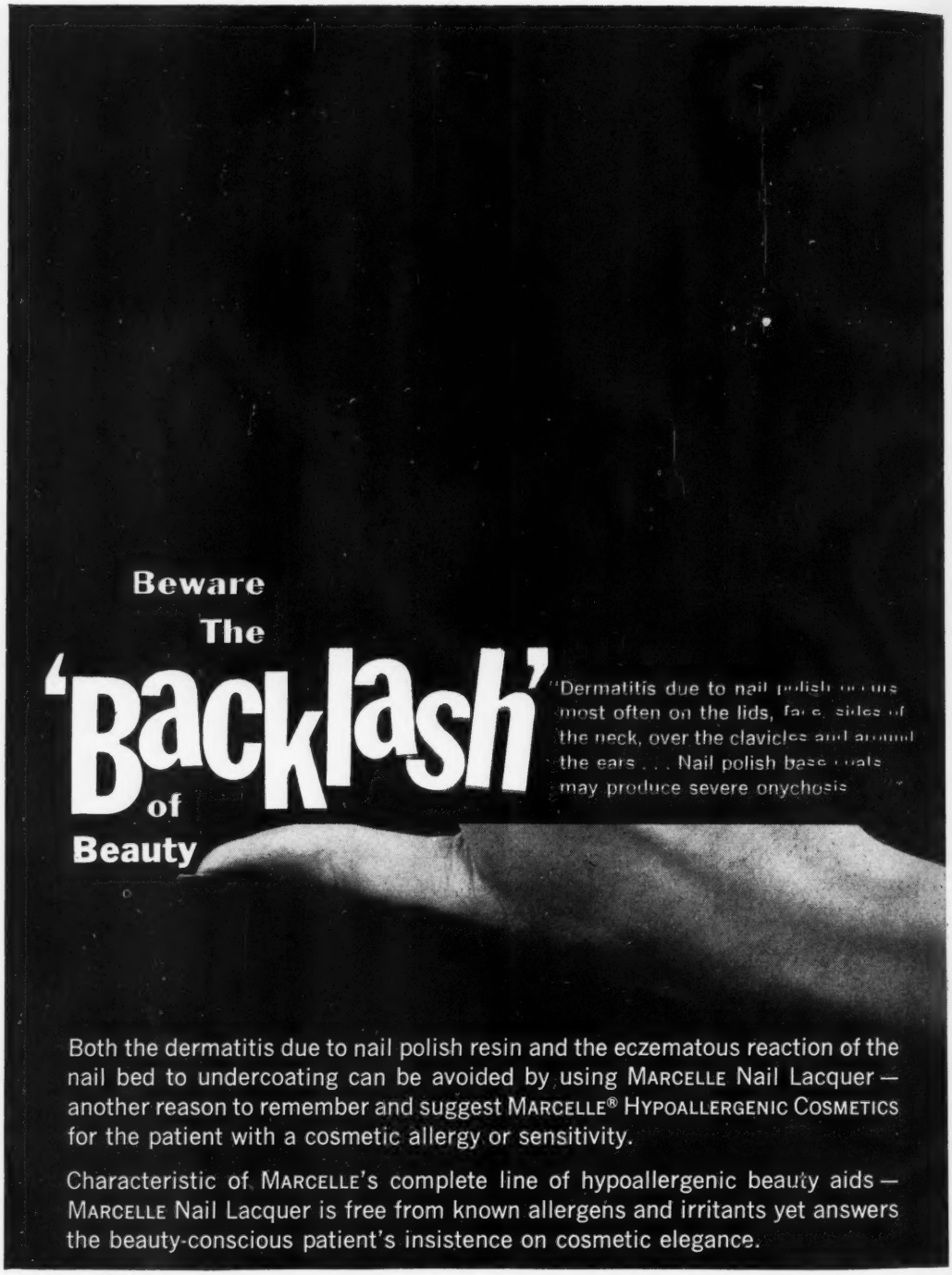
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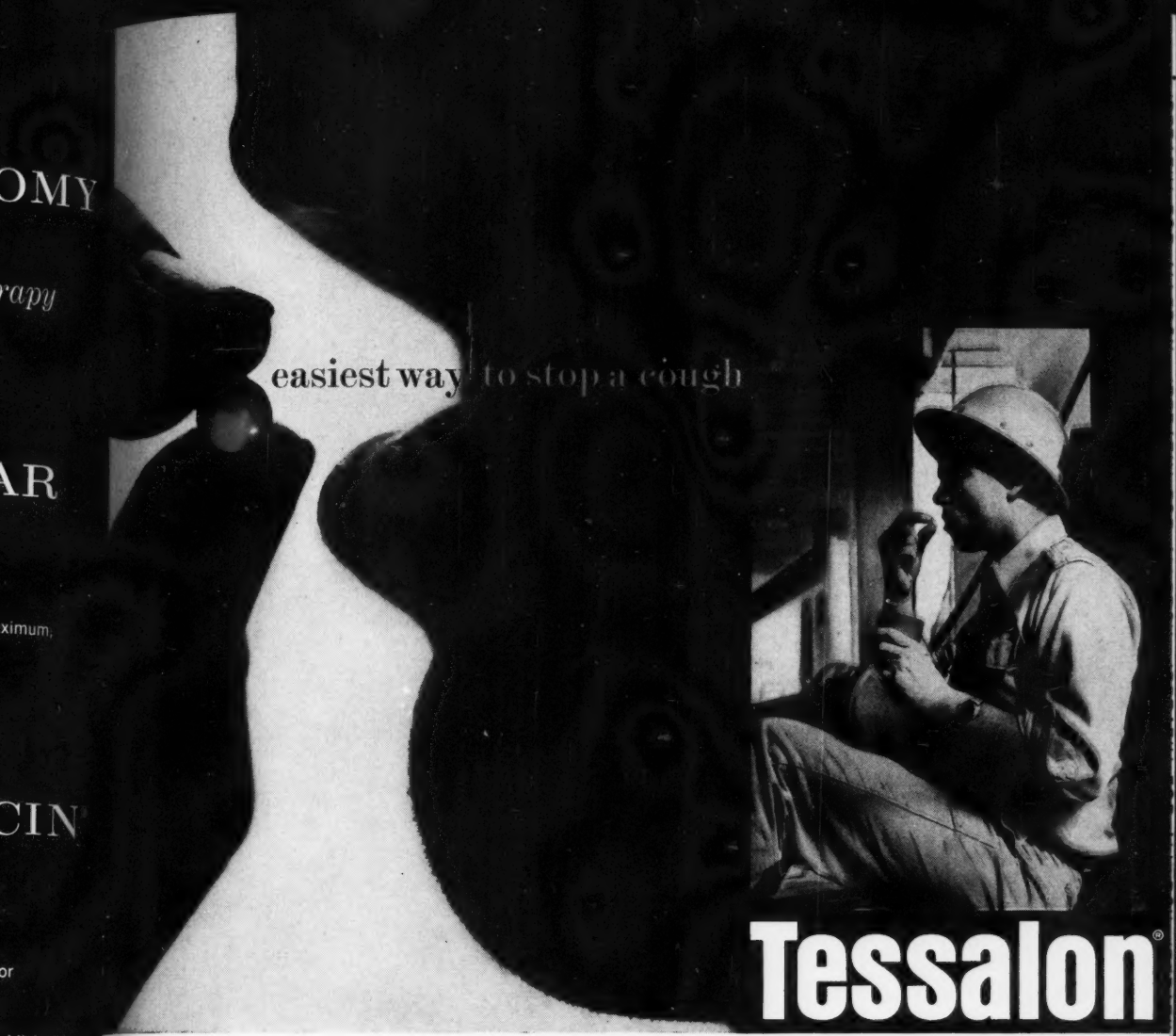

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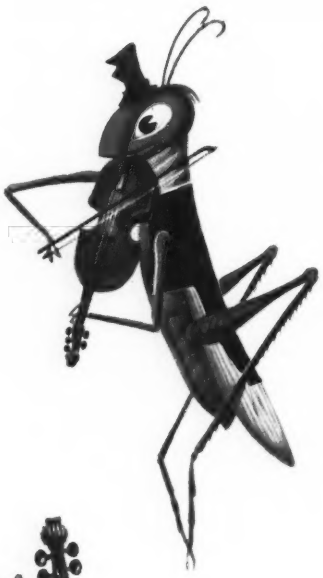


'Perazil' relieves the symptoms of sneezing "incessant" itching, inflamed eyes, rhinorrhea itching eyes, nose and throat, associated with:

- HAY FEVER
- POLLENOSIS
- PRURITUS
- URTICARIA
- VASOMOTOR RHINITIS
- ALLERGIC DERMATITIS
- DRUG SENSITIVITY

'Perazil' is both prompt and prolonged in effect providing symptomatic relief lasting 12 to 24 hours from a single dose without the high incidence of drowsiness occurring with certain antihistamines. When drowsiness does occur it is generally mild and the usual precautions should be observed. No toxic effects related to either the blood-forming organs or the cardiovascular system are produced.

DOSAGE

Adults and children over 8 years, 50 mg. once or twice daily as required. The dose may be increased in severe cases.

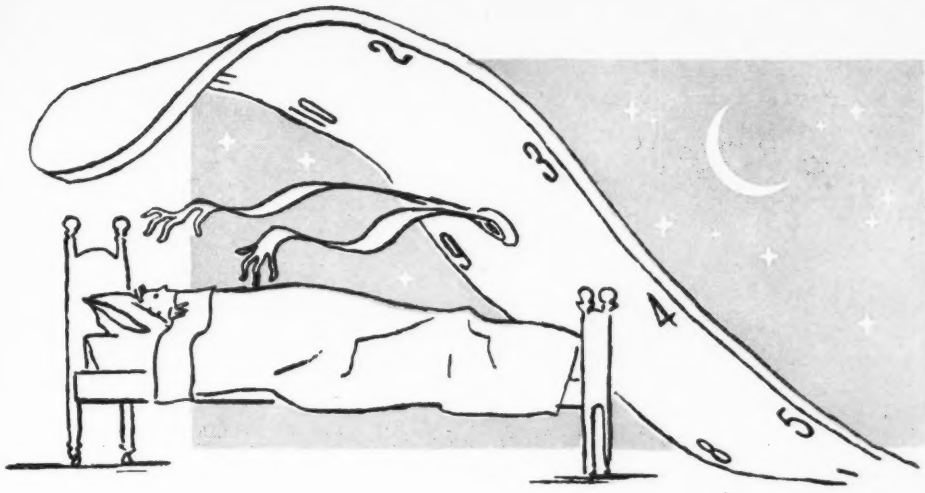
Children from 2 to 8 years, 25 mg. (one sugar-coated tablet) once daily.

Infants up to 2 years, 12½ mg. (one quarter of a 50 mg. tablet) crushed and mixed with a spoonful of jam or syrup.

'PERAZIL'® brand Chlorcyclizine Hydrochloride

Tablets of:
25 mg., sugar-coated, bottles of 100 and 1000
50 mg., scored, bottles of 100 and 1000

BURROUGHS WELLCOME & CO. (U.S.A.) INC. Tuckahoe, New Yor



Night hours need not be long for the asthmatic

The acute attack of asthma is far more terrifying at night. Keep your patient serene throughout the night, and comfortable all day, too with*

Luasmin

Luasmin capsules two or three times a day and a capsule with an enteric coated tablet at night bring your patient round the clock relief.

Each capsule or tablet contains:
Theophylline Sodium Acetate 0.2 Gm.
Ephedrine Sulfate 30 mg.
Sodium Phenobarbital 30 mg.
Supplied: Capsules and enteric coated (delayed action) tablets.
Note the adequate therapeutic dose of ephedrine balanced by the correct dose of phenobarbital.

*Ethan Allen Brown, N.E. J. Med., 223:843.

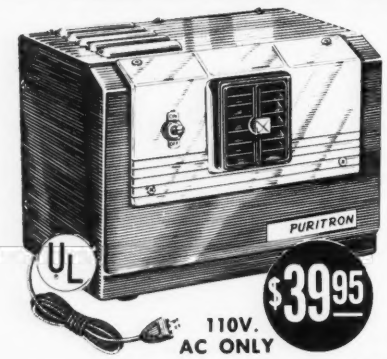
F. K. Albrecht, Mod. Mgmnt. Clin. Med., P674, Williams & Wilkins.

F. W. Wittich, J. Am. Ger. Soc., 3:239, 1955

Brewer
Est. 1852

Brewer & Company, Inc.
Worcester, Mass.

AN EFFECTIVE METHOD TO RELIEVE ASTHMA SINUS ALLERGY PATIENTS



Just plug in; it's portable!

U.S. Pat. Nos. 2,855,641 – 2,359,057
other patents pending

Hospital-accepted Puritron quickly clears any room of irritating dust, pollen, smoke and odors.

Puritron's unique filtering action pulls irritating dust, pollen and smoke out of the air . . . forces them through a superfine fiberglas filter. The air then passes through a germicidal ultra-violet light bath. This sanitizing light washes the air electronically – eliminates invisible substances that can often trigger allergic reactions.

Your patients breathe easier . . . sleep better, as Puritron circulates a constant supply of clean, Spring-fresh air – even in unventilated rooms.

Names of Hospitals Using PURITRON Furnished on Request

DOCTORS WHO TESTED PURITRON IN THEIR OWN HOMES, ON THEIR OWN FAMILIES . . . IN THEIR OFFICES AND OPERATING ROOMS REPORT:

"Within a period of one week of testing, the Puritron controlled a stubborn form of respiratory allergy in my daughter, age 5." —A Southern Physician

"Surpassed all expectations. Performs miracles for a dust allergy patient." —A Pennsylvania Physician

"For the first time I woke up without sinus trouble." —New Jersey M.D.

"I have been recommending your Puritron machine . . . Some of my patients have purchased the machine and have found it to work excellently. I myself have used it now for some time and I also can say that the machine really works pretty well." —A New England Physician

A famed New England Allergist installed three Puritrons in his offices. .

A New York physician has discovered that a Puritron in his operating room lessens the amount of mucous present.

Puritron's price: $39.95. Additional information on request.

$79.95 double-size Office Model in handsome leather-tone

ALWAYS SOLD WITH A MONEY-BACK GUARANTEE OF SATISFACTION

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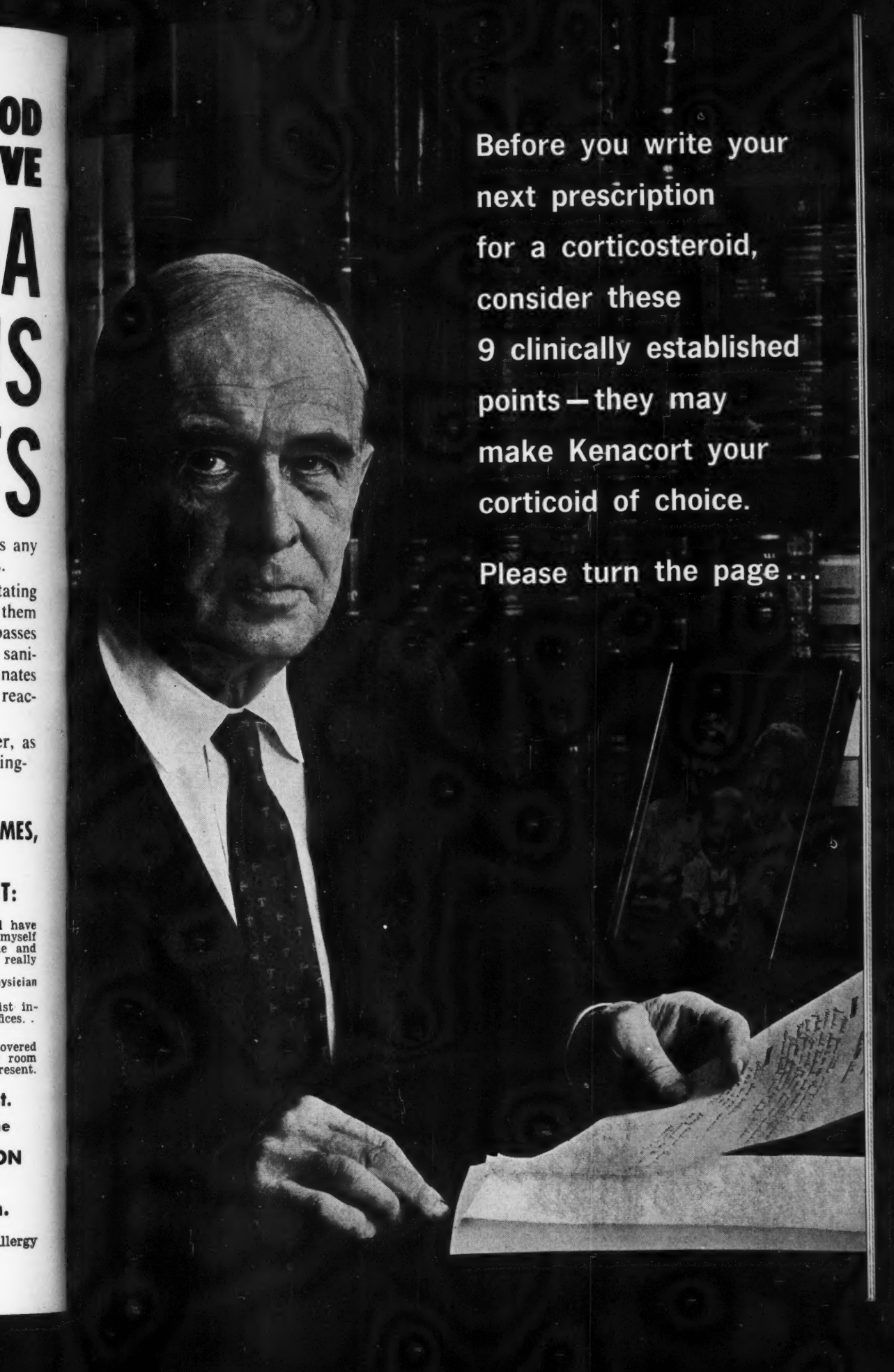
New Haven, Conn.


Before you write your
next prescription
for a corticosteroid,
consider these
9 clinically established
points—they may
make Kenacort your
corticoid of choice.
Please turn the page...

for choice corticosteroid therapy

consider...

pre-prescription point number **1**

initial therapy—remarkably free from complications

Allison, J. R., Sr., and Allison, J. R., Jr.: Monographs on Therapy 3:99 (Oct.) 1958.

pre-prescription point number **2**

continuing therapy—maintenance doses are low

Feinberg, S. M.; Feinberg, A. R., and Fisherman, E. W.: J. A. M. A. 167:58 (May 3) 1958.

pre-prescription point number **3**

no sodium or water retention—low salt diet not necessary

Hartung, E. F.: J. A. M. A. 167:973 (June 21) 1958.

pre-prescription point number **4**

absence of edema

Council on Drugs: J. A. M. A. 169:257 (Jan. 17) 1959.

pre-prescription point number **5**

less likely to create electrolyte disturbance

Bongiovanni, A. M.; Mellman, W. J., and Eberlein, W. R.: J. Pediat. 53:3 (July) 1958.

pre-prescription point number **6**

no secondary hypertension—no significant change in pulse, respiration, or blood pressure

Shelley, W. B.; Harun, J. S., and Pillsbury, D. M.: J. A. M. A. 167:959 (June 21) 1958.
Bernsten, C. A., Jr., and others: New York Rheumatism Association, Annual Meeting, New York, April 9, 1959.

... Kenacort

(SQUIBB TRIAMCINOLONE)

Available in 1 mg., 2 mg., and 4 mg. scored tablets.

pre-prescription point number **7**

no excessive appetite

Council on Drugs:
J. A. M. A. 169:257 (Jan. 17) 1959.

pre-prescription point number **8**

without unnatural psychic stimulation —does not stimulate and rarely depresses the mood

Shelley, W. B.; Harun, J. S., and Pillsbury, D. M.:
J. A. M. A. 167:959 (June 21) 1958.
Council on Drugs:
J. A. M. A. 169:257 (Jan. 17) 1959.

pre-prescription point number **9**

gastrointestinal complaints infrequent

Hartung, E. F.:
J. A. M. A. 167:973 (June 21) 1958.

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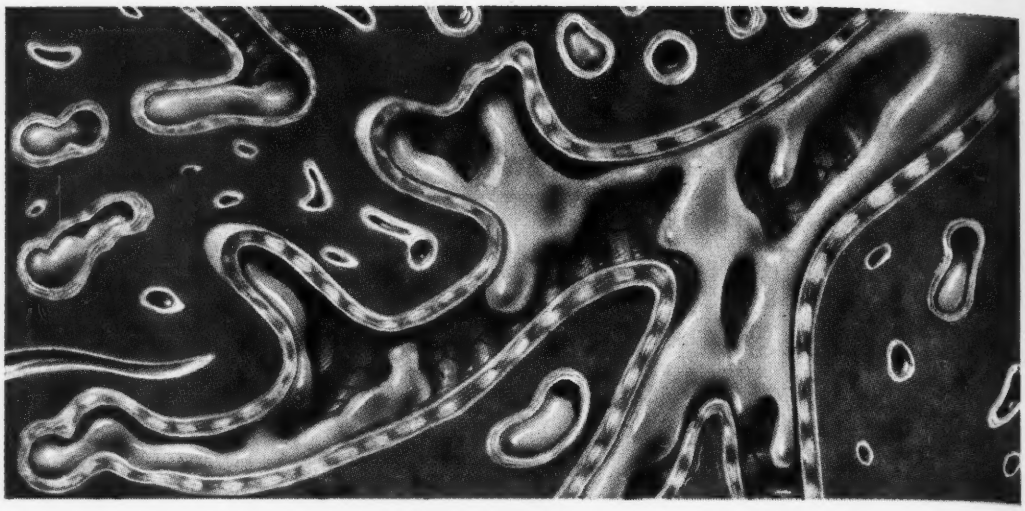
Squibb Quality — the Priceless Ingredient

'KENACORT'® IS A SQUIBB TRADEMARK



LIQUEFIES THICK TENACIOUS MUCUS ON CONTACT

Dornavac®

PANCREATIC DORNASE

- DORNAVAC starts on contact to reduce tenacity and viscosity of mucopurulent bronchial secretions.
- DORNAVAC specifically lyses desoxyribonucleoprotein, which constitutes 30 to 70 per cent of purulent bronchial exudates. Striking clinical improvement often begins within 30 minutes after aerosol therapy.
- DORNAVAC has no enzymatic effect on living tissue. It is well tolerated and compatible with antibiotics.

Indications: purulent bronchitis, bronchiectasis, atelectasis, emphysema, unresolved pneumonia and chronic bronchial asthma.

Supplied: Each combination package contains one vial of lyophilized pancreatic dornase (100,000 units) and one 2 cc. vial of sterile diluent.

for inhalation therapy in bronchopulmonary disease

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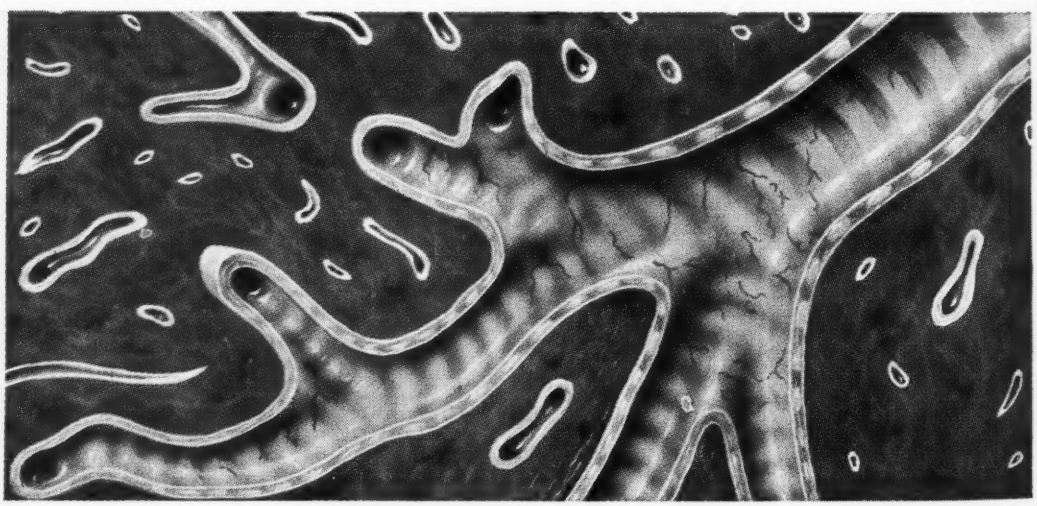
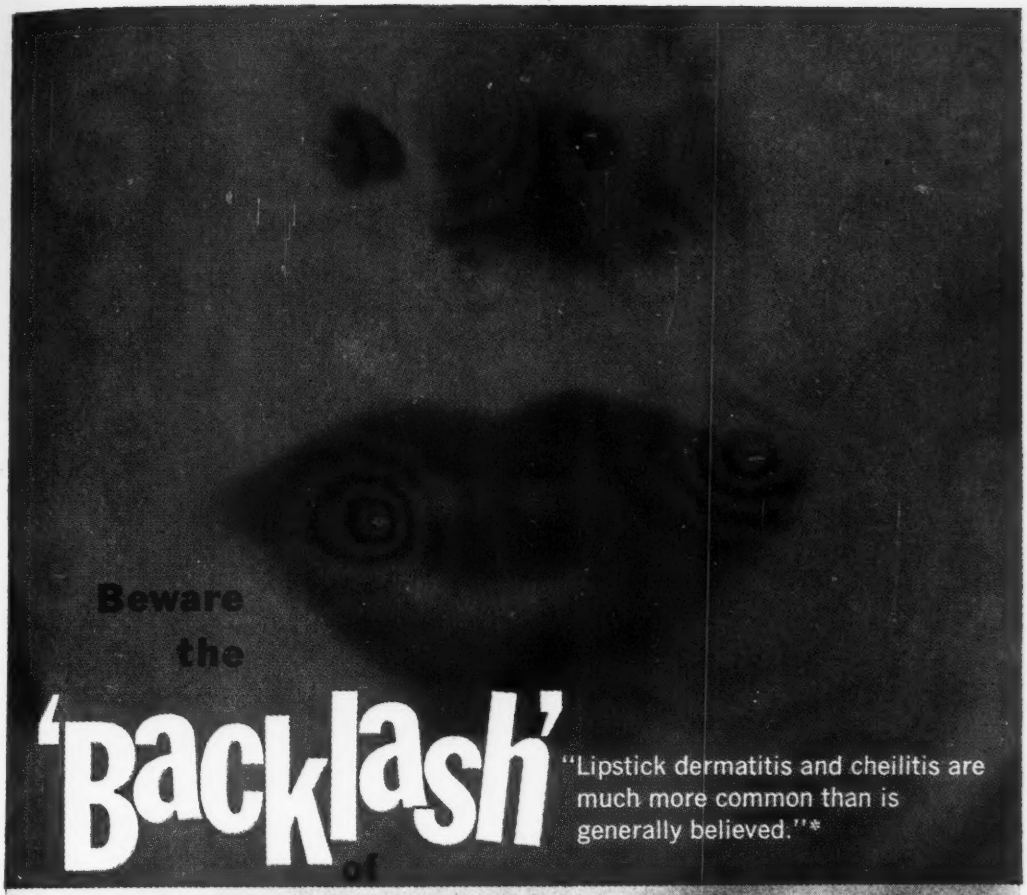
Additional information is available to physicians on request. Address Professional Service Department, West Point, Pa.





Beware the

'Backlash' of Beauty

"Lipstick dermatitis and cheilitis are much more common than is generally believed."*

Dermatoses resulting from sensitivity to a variety of lipstick ingredients can be avoided by using MARCELLE Lipsticks — another reason to remember and suggest MARCELLE® HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.

MARCELLE Lipsticks — available in a full range of colors — are offered in different formulas to eliminate common sensitizers, and to avoid perfumes and the bromofluoresceins. The MARCELLE Lipstick Testing Kit, providing 14 different formulations, enables you to help your patient select a lipstick best suited to her case.

Marcelle COSMETICS

Borden's PHARMACEUTICAL DIVISION
350 Madison Avenue, New York 17

Available in Canada through Prof. Sales Corp., Montreal

*Zakon, S. J., et al.: Arch. Dermat. & Syph. 56:499, 1947; abstracted in Birmingham, D. J., and Campbell, P. C., Jr.: Occupational and Related Dermatoses, U. S. Public Health Service Publication No. 364, 1954.

Prompt—Long-lasting—Economical

QUADRINAL

- **bronchodilator and expectorant**

QUADRINAL

- **bronchial asthma**

QUADRINAL

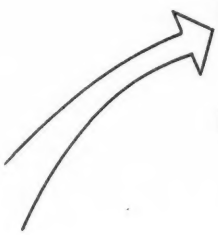
- **pulmonary emphysema**

QUADRINAL

- **other chronic respiratory disease with bronchospasm and wheezing**

FORMULA:

Ephedrine HCl	3/8 grs. (24 mg.)
Phenobarbital	3/8 grs. (24 mg.)
"Phyllicin" (theophylline-calcium salicylate)	2 grs. (120 mg.)
Potassium iodide	**5 grs. (0.3 Gm.)**



DOSAGE: The usual dose of **QUADRINAL** is 1 tablet every three or four hours during the day and, if needed, another tablet upon retiring for relief during the night.

For children, ½ tablet three times a day.

QUADRINAL is available on prescription only.

QUADRINAL tablets (7-¾ grs. each) bottles of 100, 500, and 1000.

Quadrinal, Phyllicin®, E. Bilhuber, Inc.

KNOLL PHARMACEUTICAL COMPANY
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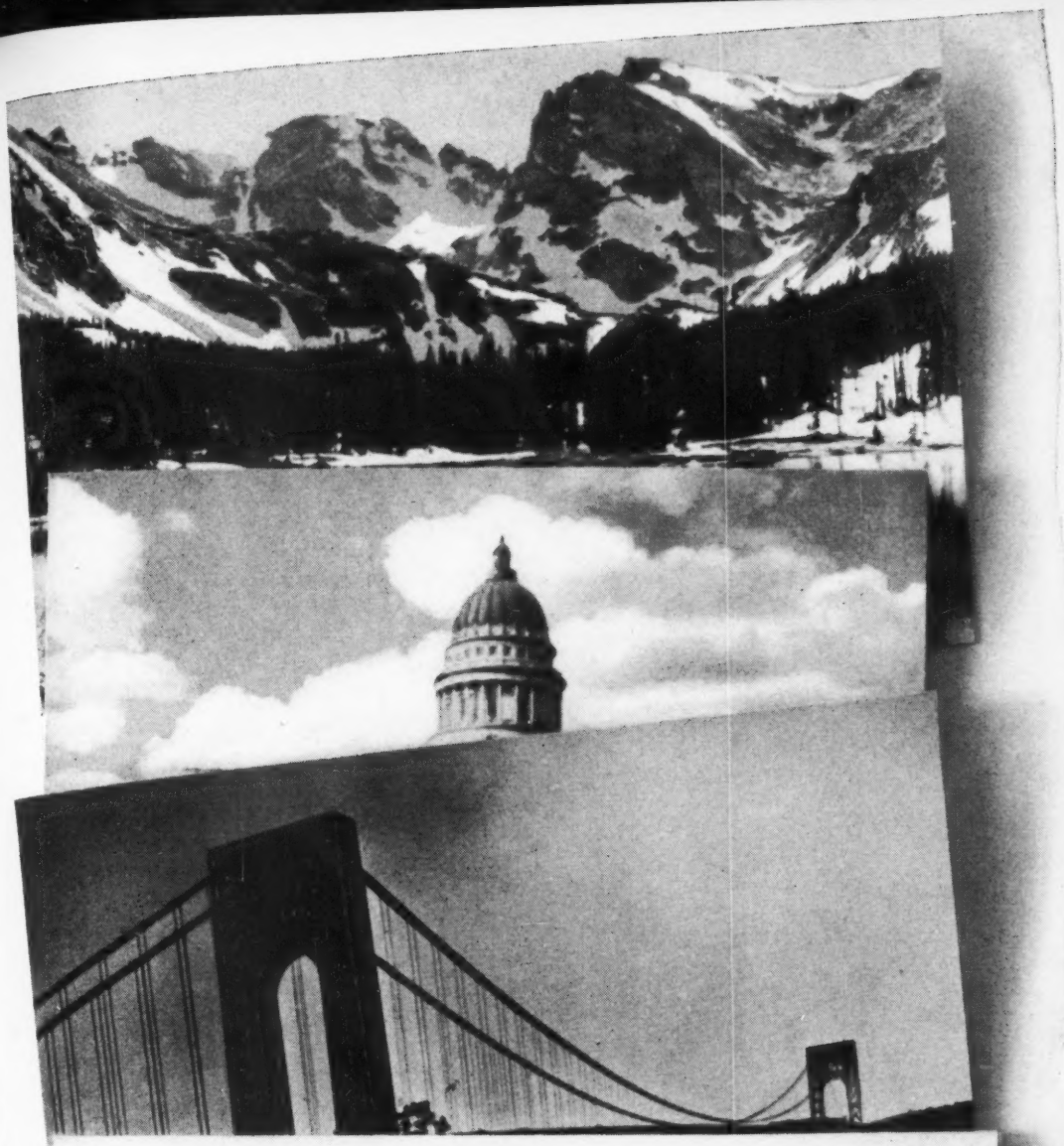
Orange, New Jersey



Polaramine — the closest to a perfect antihistamine — offers four major benefits to provide your patients with greater freedom from seasonal and nonseasonal allergies.

Greater therapeutic response ... daylong or nightlong relief with a single 4 mg. Polaramine Repetab. Greater protection at lower dosages than with other antihistamines. Greater safety... highest therapeutic index (3380) of all antihistamines. Greater freedom from side effects. 4 mg. Polaramine Repetabs, in bottles of 100 and 1000.

POLARAMINE® Maleate, brand of dextro-chlorpheniramine maleate.
REPETABS,® Repeat Action Tablets.

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SYMBOL OF THE ONE-DOSE CONVENIENCE YOU WANT FOR YOUR PATIENT

PROMPT REPETAB RELIEF · LASTS ALL DAY OR NIGHT ·

Wherever the 4 winds blow... new 4 mg.

POLARAMINE REPETABS

for relief of allergic reactions and day-to-day maintenance

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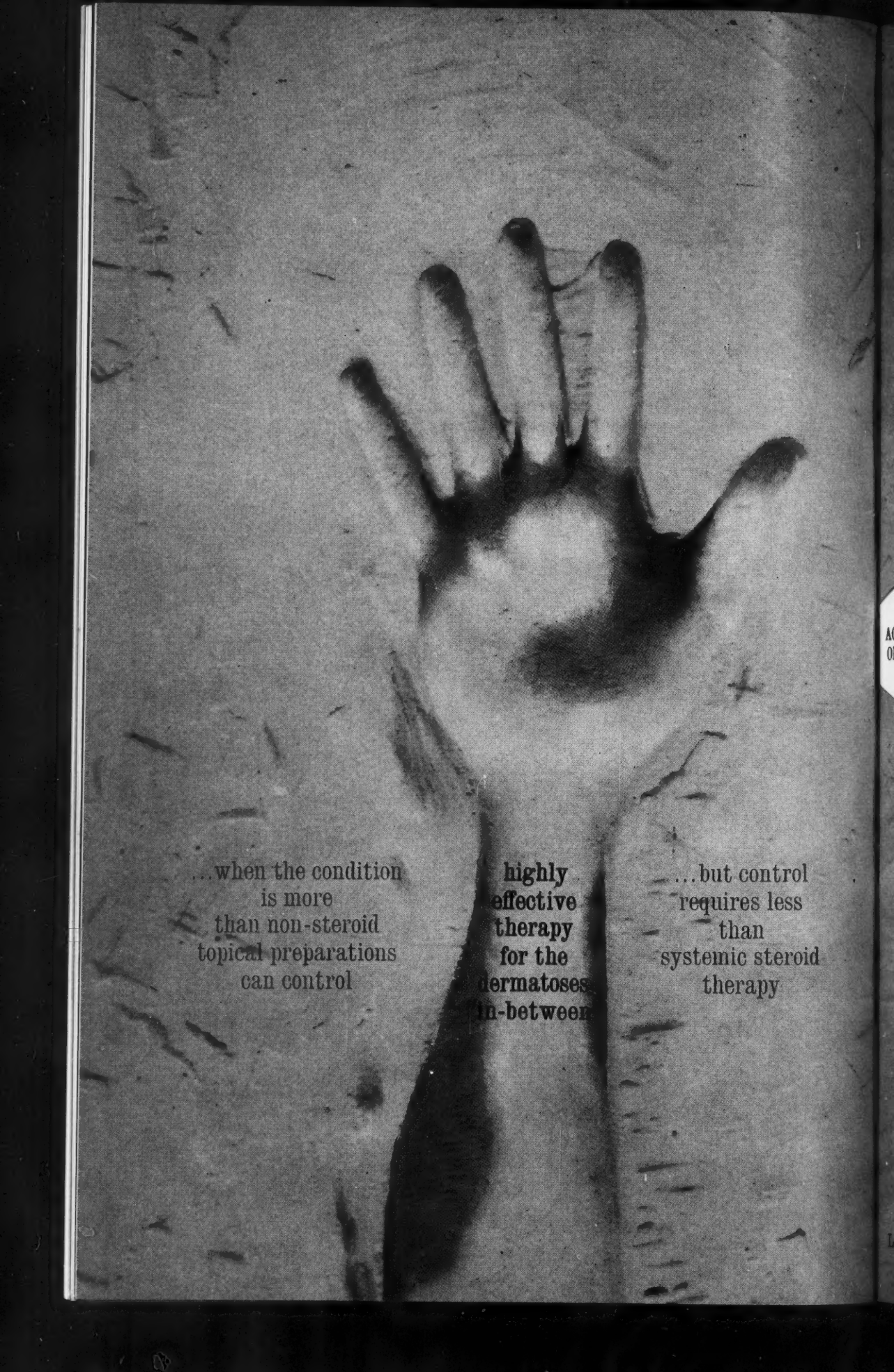

...when the condition is more than non-steroid topical preparations can control
highly effective therapy for the dermatoses in-between
...but control requires less than systemic steroid therapy

In the experience of leading investigators, triamcinolone acetonide has proved itself one of the most effective topical corticosteroids yet introduced.*

*Baer, R. L., and Witten, V. H.: Editorial Comment. In The Year Book of Dermatology and Syphilology (1958-1959 Year Book Series). Edited by Rudolph L. Baer and Victor H. Witten, Chicago, The Year Book Publishers, 1959, p. 40.

inflammatory, allergic skin conditions

ACETONIDE OINTMENT

Aristocort

ACETONIDE CREAM

TRIAMCINOLONE ACETONIDE 0.1%
TUBES OF 5 GM. AND 15 GM.

either...sparingly applied...offers the unsurpassed efficacy of Aristocort in topical situations...with 10-fold the potency of hydrocortisone topically yet without the hazards associated with systemic absorption.

new...for inflammatory, allergic, infective eye and ear conditions

Neo-Aristocort Eye-Ear Ointment

Triamcinolone Acetonide 0.1%—Neomycin Sulphate 0.5%
Tubes of ⅛ oz.

Lederle

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, N.Y.

B.A.C.

For the Prevention and Treatment of Recurring Upper Respiratory Infections and Infectious Asthma

B.A.C.—Acellular Bacterial Antigen Complex—although derived from bacteria, is not a cellular vaccine. Prepared by the special Hoffmann process of coprecipitation, it provides the specific protective substances of the bacterial cell *plus* the toxins and metabolites. Standardized to uniform potency, B.A.C. is an acellular, water-clear solution, essentially free of sensitizing extraneous components, and is not liable to deterioration on keeping, with resultant loss of antigenic properties.

B.A.C. avoids the pitfalls of antibiotic therapy—Stimulates immune body formation, avoids development of resistant bacteria and superinfections and liability to allergic reactions.

B.A.C. provides important antigens lacking in cellular vaccines—Vaccines lack important specific surface antigenic factors and are deficient in exotoxins and other antigenic metabolites.

B.A.C. combines the essential immunogenic factors for maximum immunologic response.

B.A.C. acts to improve the natural defense mechanisms—The action of B.A.C. is immunologically natural, namely, stimulation of the host's defense against bacterial invaders.

B.A.C. affords prompt, effective and safe therapy—Controlled clinical studies[1-5] in both children and adults have consistently shown favorable response in more than 80 per cent of cases of upper respiratory infection and infectious asthma. Significant side effects have been rarely noted and are eliminated by dilution of the antigen.

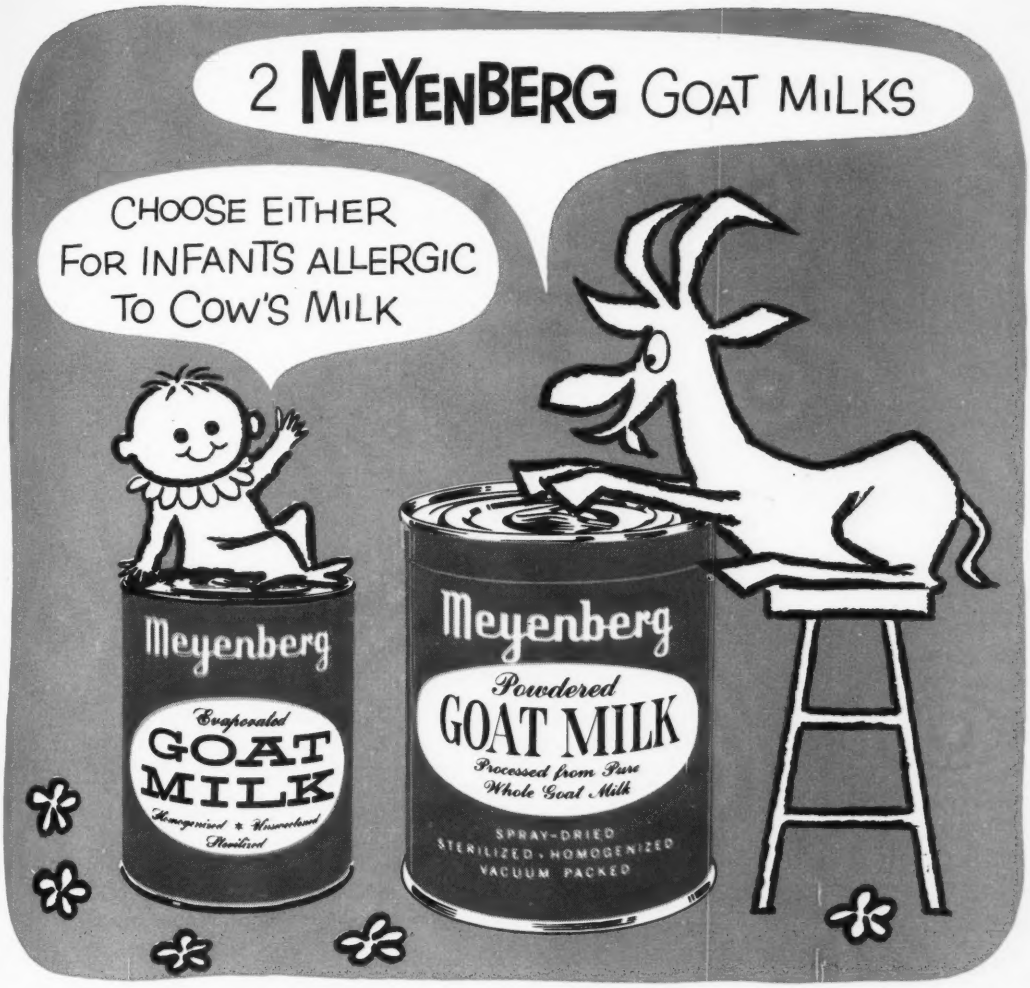
B.A.C. is available in multiple dose vials in several different combinations for broad-spectrum immunization. Complete information on B.A.C. preparations, clinical experience, and dosage will be supplied on request.

1. Spielman, A. D.: New York J. Med. *55*:1603 (June 1) 1955.
2. Shinefield, M. A.: New York J. Med. *56*:1466 (May 1) 1956.
3. Dalven, J., and Romano, F. J.: New York J. Med. *57*:1748 (May 15) 1957.
4. Gundy, J. E.: J. Pediat. *51*:516 (Nov.) 1957.
5. Spielman, A. D.: A.M.A. Arch. Otolaryng. *67*:204 (Feb.) 1958.

ACELLULAR B.A.C. HOFFMANN

Hoffmann Laboratories, Inc.

666 Broadway, Paterson 4, N. J.



EVAPORATED OR POWDERED, Meyenberg Goat Milk is nutritionally equal to cow's milk in carbohydrates, protein and fat. And since the offending antigen in cow's milk is usually lactalbumin (a species protein), goat milk has often proved a successful substitute for cow's milk. Therefore, the infant is not deprived of the irreplaceable values of milk, as may occur when synthetic milk formulas are fed. *Recent clinical findings indicate there are nutritive values in natural animal milk that are lacking in synthetic preparations.**

In addition, Meyenberg Goat Milk is free of crude fibers and other extraneous material which may cause digestive upset. Gastrointestinal disturbances with abnormal stools, diarrhea, sore buttocks, cramping and occasional vomiting have been reported* following the ingestion of soy preparations. Thus, for infants allergic to cow's milk, prescribe Meyenberg Goat Milk *first* – either Evaporated or Powdered.

Always prescribe Meyenberg – the standard for highest, most dependable quality since 1934.

FULL-SIZE TRIAL CAN ON REQUEST.
Powdered in 14 oz. cans, evaporated in 14 fl. oz. cans.

JACKSON-MITCHELL *Pharmaceuticals, Inc.*

10401-C Virginia Ave., Culver City, Calif.

*FRIES, J. H., MILK ALLERGY – DIAGNOSTIC ASPECTS AND THE ROLE OF MILK SUBSTITUTES, J.A.M.A., NOV. 23, 1957.

Atopic dermatitis before treatment

NOW...

to relieve inflammation fas

- mg. for mg. the most active steroid topically—up to 40 times the poten of hydrocortisone
- optimal not minimal steroid concentration for peak effectiveness... m imal contact at the site of the lesion
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- no irritating steroid particles, no sting, stain, smell, stickiness

After treatment ACTUAL CLINICAL PHOTOGRAPHS

TOPICAL CREAM

NeoDecadron*

DEXAMETHASONE 21-PHOSPHATE—NEOMYCIN SULFATE

ICATIONS: Allergic or inflammatory dermatoses, with or ithout pruritus; sunburn; insect bites; otitis externa nly if the drum is intact).

UTION: Steroids should not be used in the presence of berculosis of the skin.

AGE: A small quantity of NeoDECADRON Topical Cream 1%) is applied to the affected area 2-3 times daily.

dditional information is available to physicians on request.

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	ACTIVE INGREDIENTS			
Product	Steroid Concentration	Dexamethasone 21-Phosphate (as disodium salt)	Neomycin Sulfate	Supplied
NeoDECADRON Topical Cream	0.1%	1 mg./Gm.	5 mg./Gm. (equivalent to 3.5 mg. neomycin base)	5 Gm. (⅙ oz.) tube 15 Gm. (½ oz.) tube
DECADRON® Phosphate	0.1%	1 mg./Gm.	—	5 Gm. (⅙ oz.) tube 15 Gm. (½ oz.) tube

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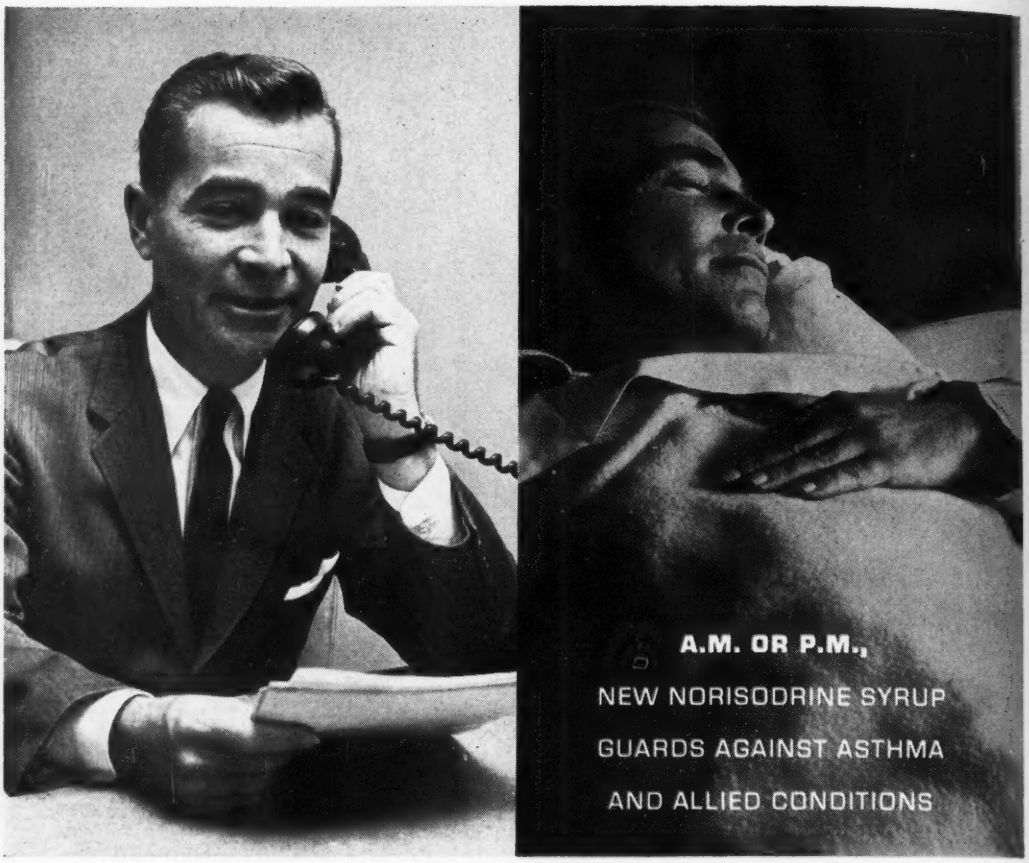

Around the clock, new Norisodrine Syrup provides prophylaxis against asthmatic attacks . . . effectively treats the bronchitic or allergic cough. Combining bronchodilator (Norisodrine Sulfate) and liquefying (Calcium Iodide) effects, this unique new form of Norisodrine offers long-term maintenance for chronic respiratory allergies.

With its pleasant-tasting honey-mint flavor, Norisodrine Syrup is especially appealing to youngsters. Supplied in pint bottles. For detailed literature, ask your Abbott man. Or write Abbott Laboratories at North Chicago, Illinois.

NORISODRINE® SYRUP
(Isoproterenol Sulfate, Abbott)

WITH CALCIUM IODIDE

ABBOTT

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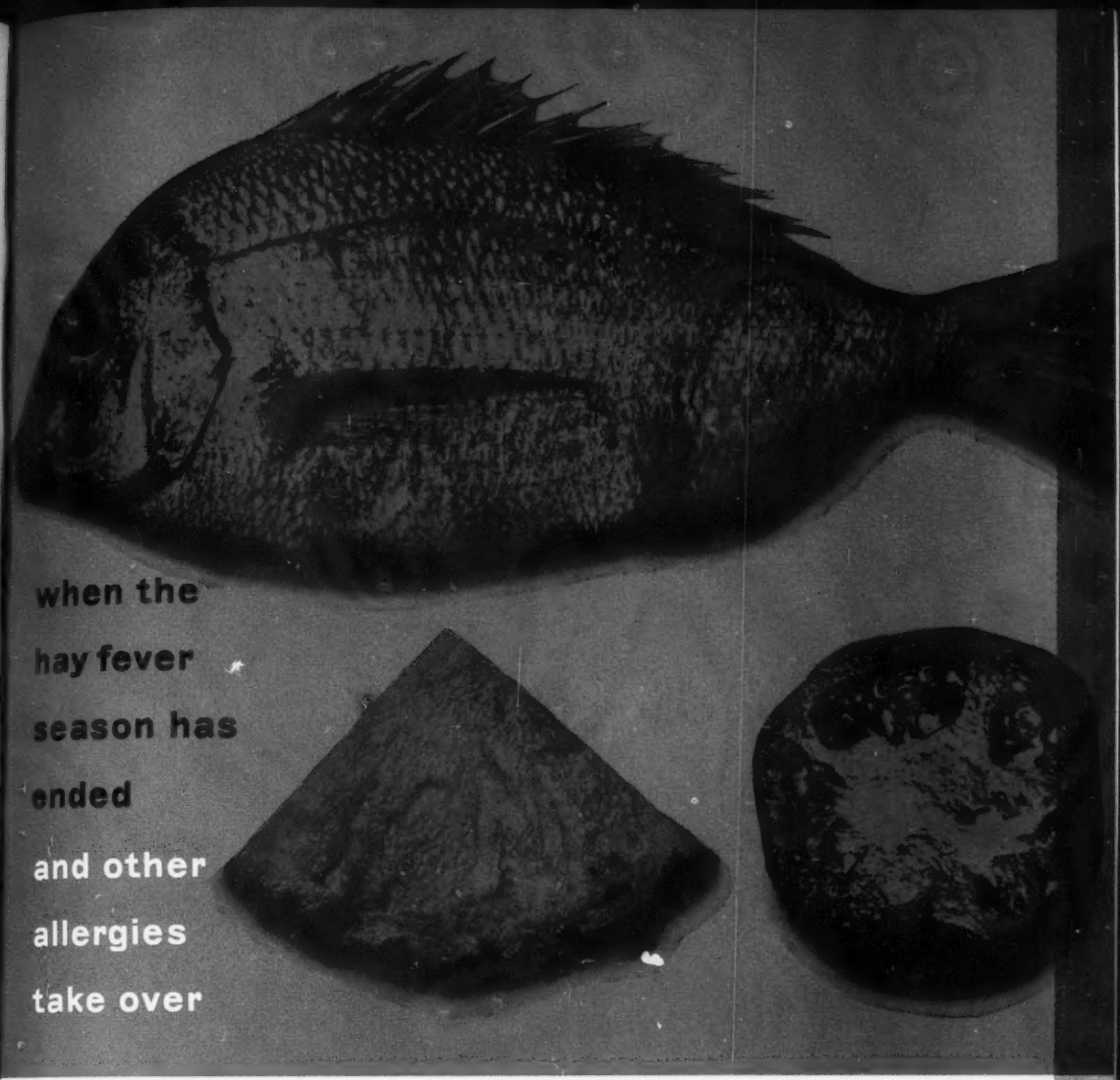

METRETON

"Meti" steroid-antihistaminic

for rapid relief systemically— METRETON Tablets—
in drug reactions, urticaria, angioedema, atopic and contact dermatitis, allergic eczema, ocular allergies, serum sickness

topically for allergic rhinitis— METRETON Nasal Spray

topically for eye allergies—
METRETON Ophthalmic Suspension

supplied

METRETON® Tablets, bottles of 30 and 100. Each METRETON Tablet contains 2.5 mg. prednisone, 2 mg. chlorprophenpyridamine maleate, and 75 mg. ascorbic acid.

METRETON Nasal Spray, 15 cc. squeeze bottle. Each cc. of METRETON Nasal Spray contains 2 mg. (0.2%) prednisolone acetate and 3 mg. (0.3%) chlorprophenpyridamine gluconate.

METRETON Ophthalmic Suspension, 5 cc. dropper bottle. Each cc. of METRETON Ophthalmic Suspension contains 2 mg. (0.2%) prednisolone acetate and 3 mg. (0.3%) chlorprophenpyridamine gluconate.

Meti,® brand of corticosteroids.

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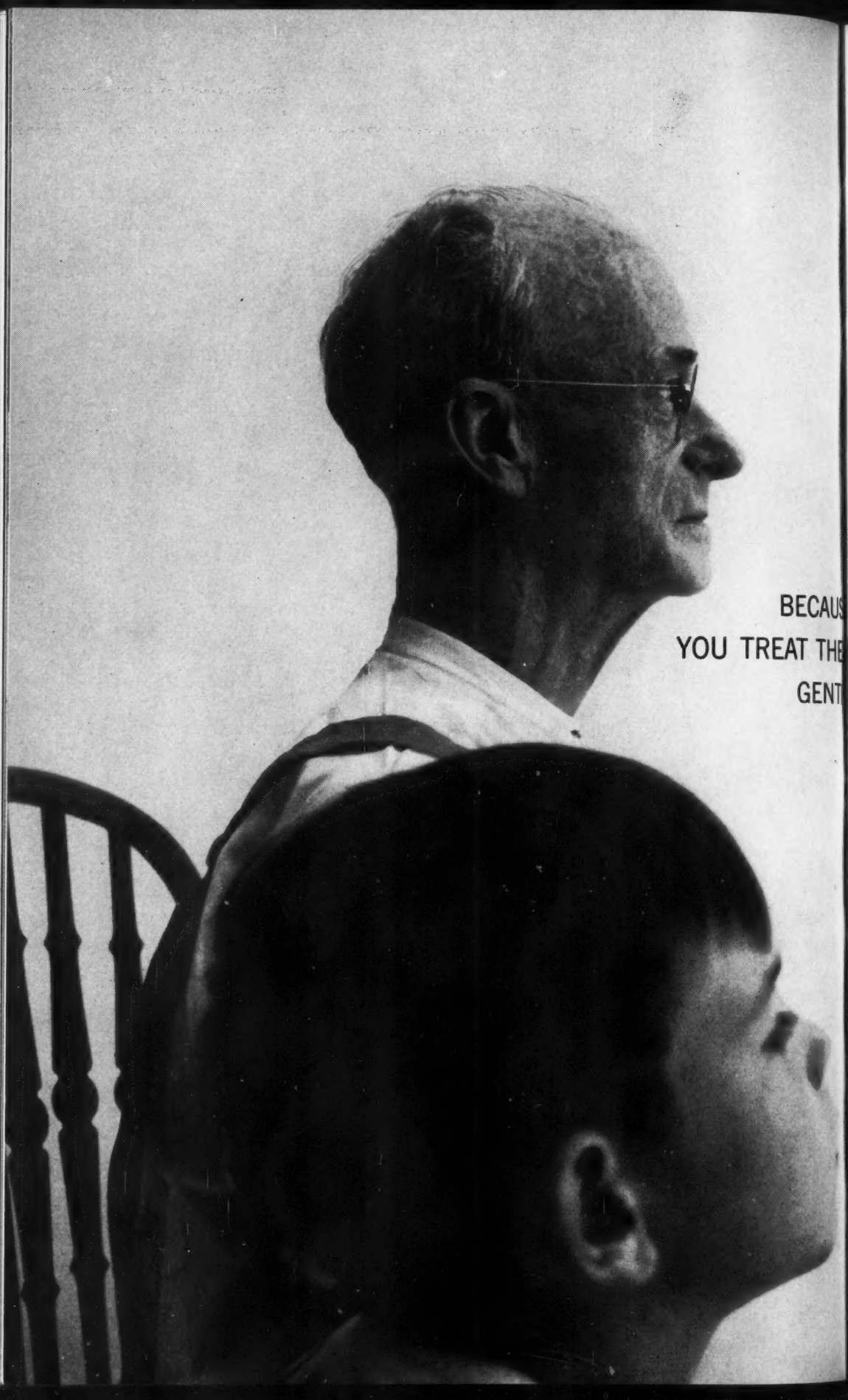
S-312


BECAUS
YOU TREAT THE
GENT

"In no case...
was there any rebound congestion."[1]

Your youngest patient as well as your oldest will find new Otrivin an unusually gentle yet remarkably effective nasal decongestant. Otrivin works quickly; its action is prolonged. Typical of many clinicians' reports is the one published by Kolodny[1]: Of 64 patients studied, 92 per cent had good or excellent results. "In no case studied was there any rebound congestion. Local side effects were minimal. . . . Extremely few systemic effects occurred. . . ."

NEW
OTRIVIN® FOR GENTLE RELIEF OF STUFFY NOSE
ON PRESCRIPTION ONLY

Otrivin is safe even for the very young. "The particularly striking feature of Otrivin solution was the absence of side effects, even in infants as young as two weeks."[2] "It is effective in low concentrations and is a safe nasal vasoconstrictor for even the young patient."[3]

SUPPLIED: Otrivin *Nasal Solution*, 0.1%; dropper bottles of 1 ounce. Otrivin *Nasal Spray*, 0.1%; plastic squeeze tubes of 15 ml. Otrivin *Pediatric Nasal Spray*, 0.05%; plastic squeeze tubes of 15 ml.

REFERENCES: 1. Kolodny, A. L.: Antibiotic Med. *6*:452 (Aug.) 1959. 2. Davis, M. R.: To be published. 3. Peluse, S.: In press.

Otrivin® hydrochloride (xylometazoline hydrochloride CIBA) 2/2753MK

CIBA SUMMIT N. J.

when holiday dinners include food allergens

BENADRYL®

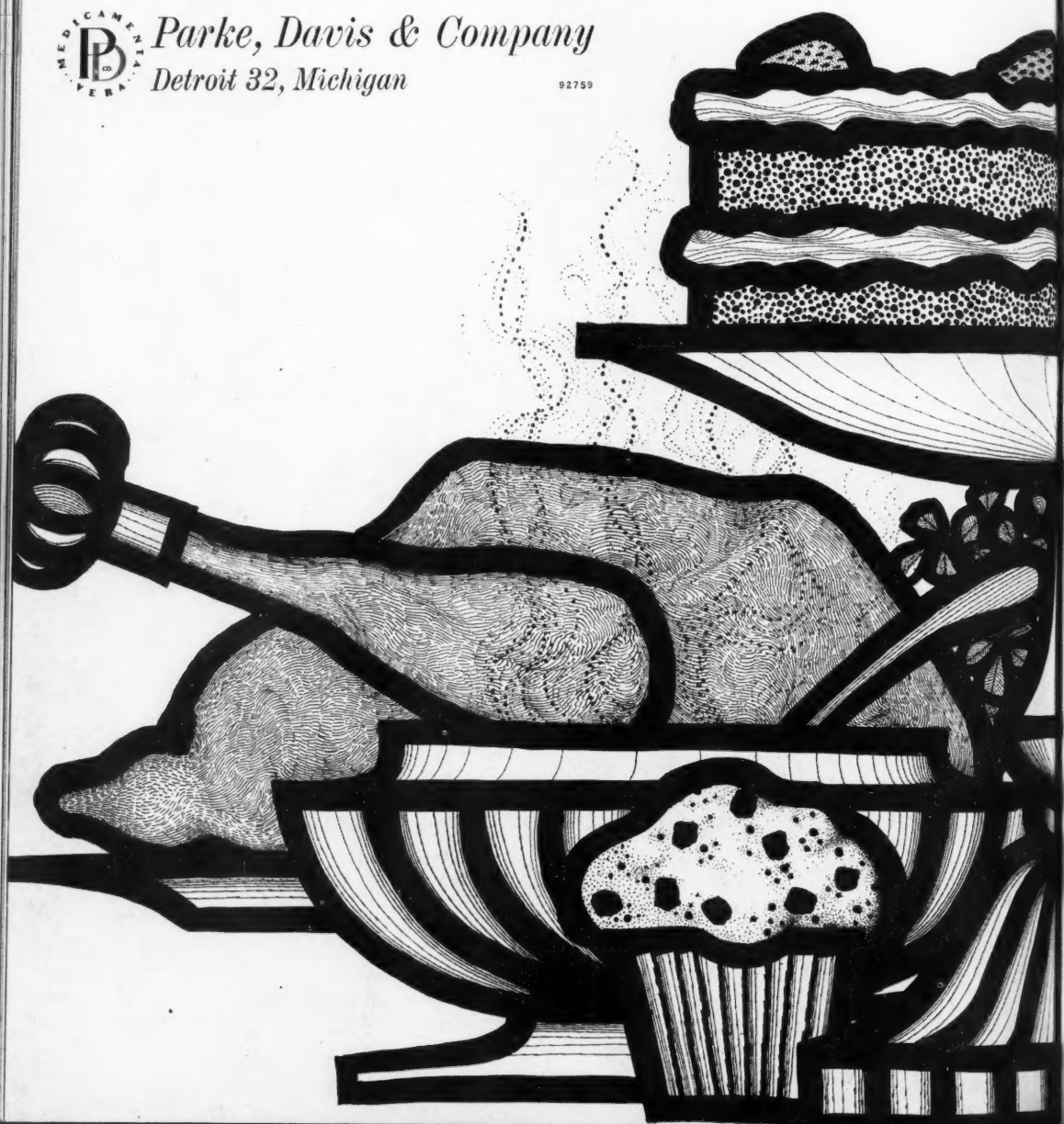
ANTIHISTAMINIC-ANTISPASMODIC

gives prompt, comprehensive relief

The patient allergic to certain foods may find holiday menus a temptation difficult to resist. When he yields to allergenic dishes, BENADRYL brings him prompt relief from gastrointestinal distress. BENADRYL also helps to control cutaneous reactions and respiratory symptoms so often associated with food sensitivity. BENADRYL Hydrochloride (diphenhydramine hydrochloride, Parke-Davis) is available in a variety of forms, including Kapseals,® 50 mg. each; Kapseals, 50 mg., with ephedrine sulfate, 25 mg.; Capsules, 25 mg. each; Elixir, 10 mg. per 4 cc.; and for delayed action, Emplets,® 50 mg. each. For parenteral therapy, BENADRYL Hydrochloride Steri-Vials,® 10 mg. per cc.; and Ampoules, 50 mg. per cc.

Parke, Davis & Company
Detroit 32, Michigan

92759



no asthma symptoms—Prophylactic use of Tedral in any of its 5 convenient dosage forms permits most bronchial asthma patients to breathe normally, live actively, avoid social embarrassment. Tedral keeps patients safely free of constriction, congestion and apprehension. When attacks are frequent, prescribe 1 or 2 plain Tedral tablets q.4.h. plus an additional tablet at the first sign of symptomatic breakthrough. Tedral protects up to 4 hours.

Formula: Each scored, plain Tedral tablet contains: Phenobarbital, 8 mg. (⅛ gr.) (Warning: May be habit forming); Theophylline, 130 mg. (2 gr.); Ephedrine, HCl 24 mg. (⅜ gr.)

TEDRAL®

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Decadron* DEXAMETHASONE

treats more patients more effectively

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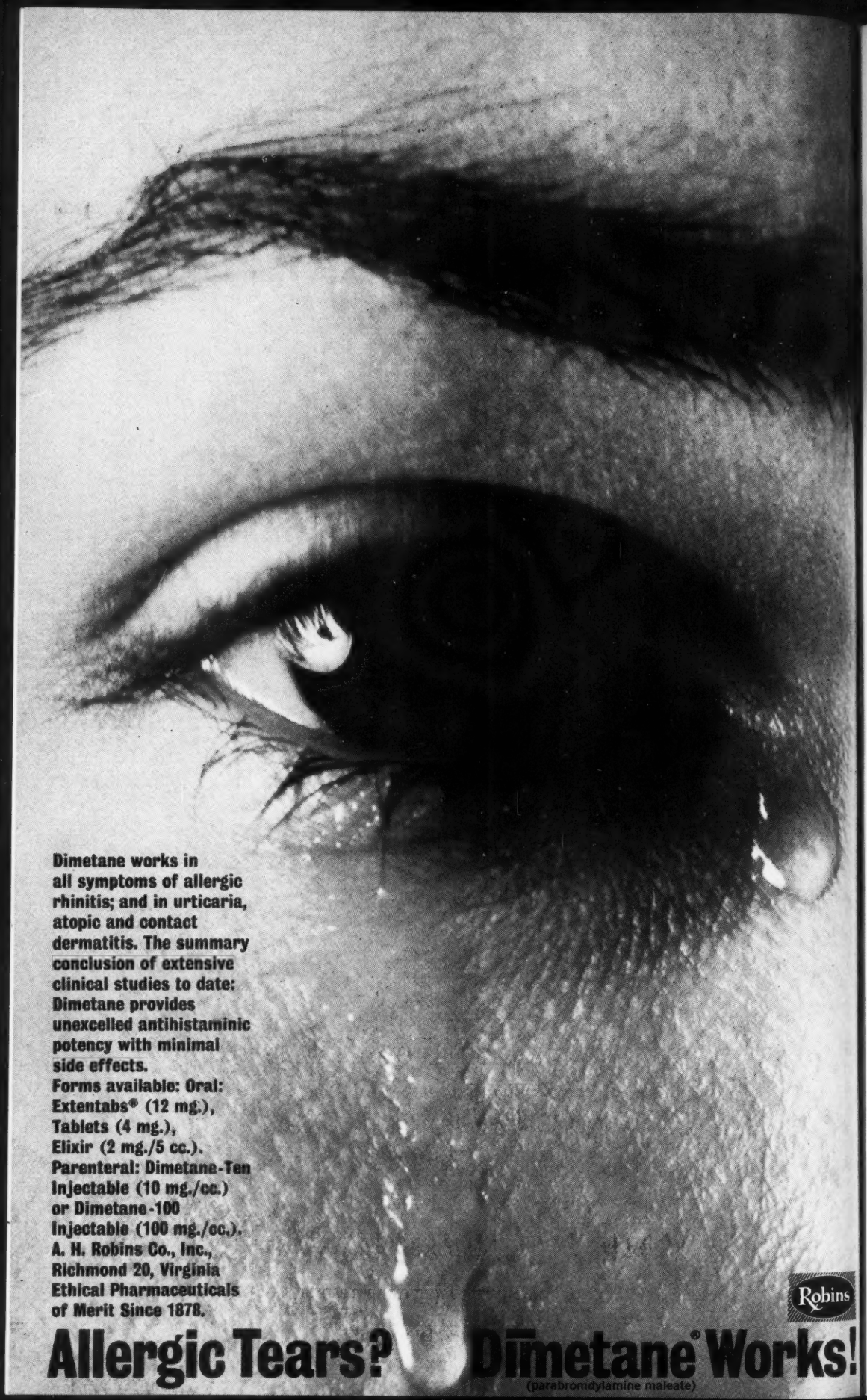

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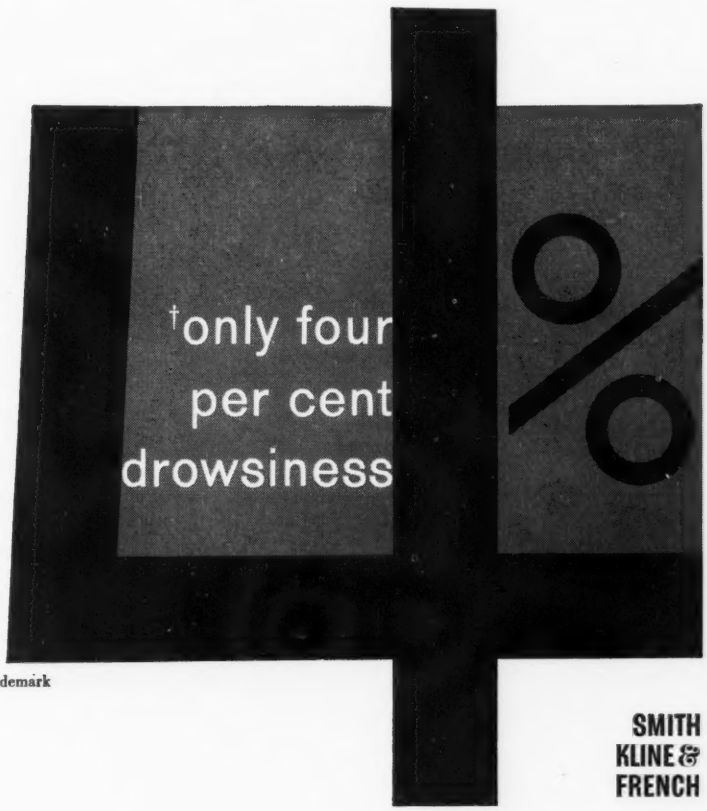

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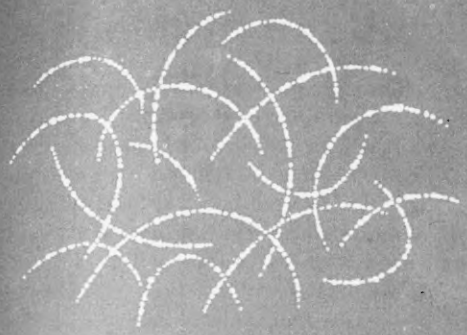

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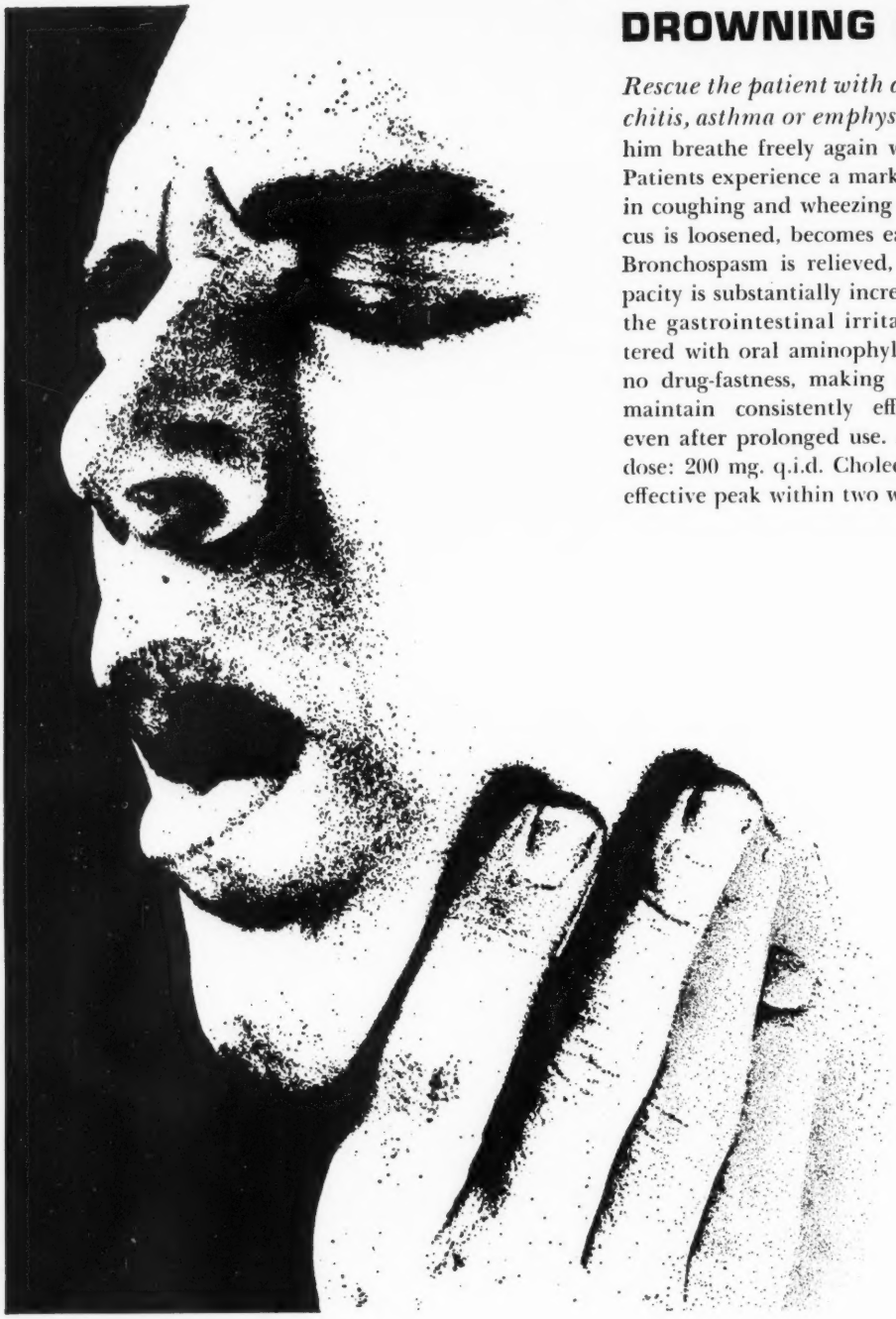

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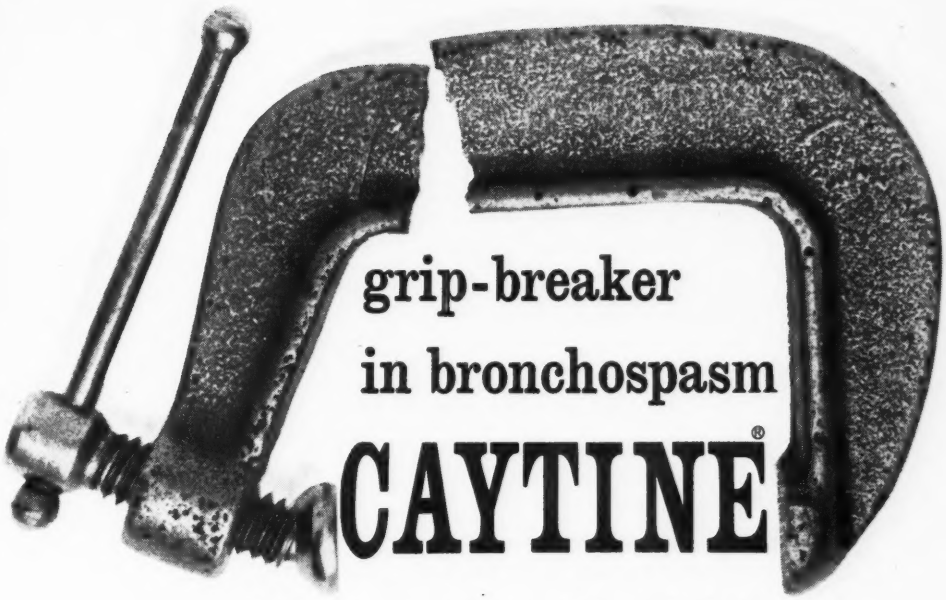

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(1) Leslie, A., and Simmons, D. H.: Am. J. M. Sc. *234*:321, 1957. (2) Settel, E.: Am. Pract. & Digest Treat. *8*:1249, 1957.

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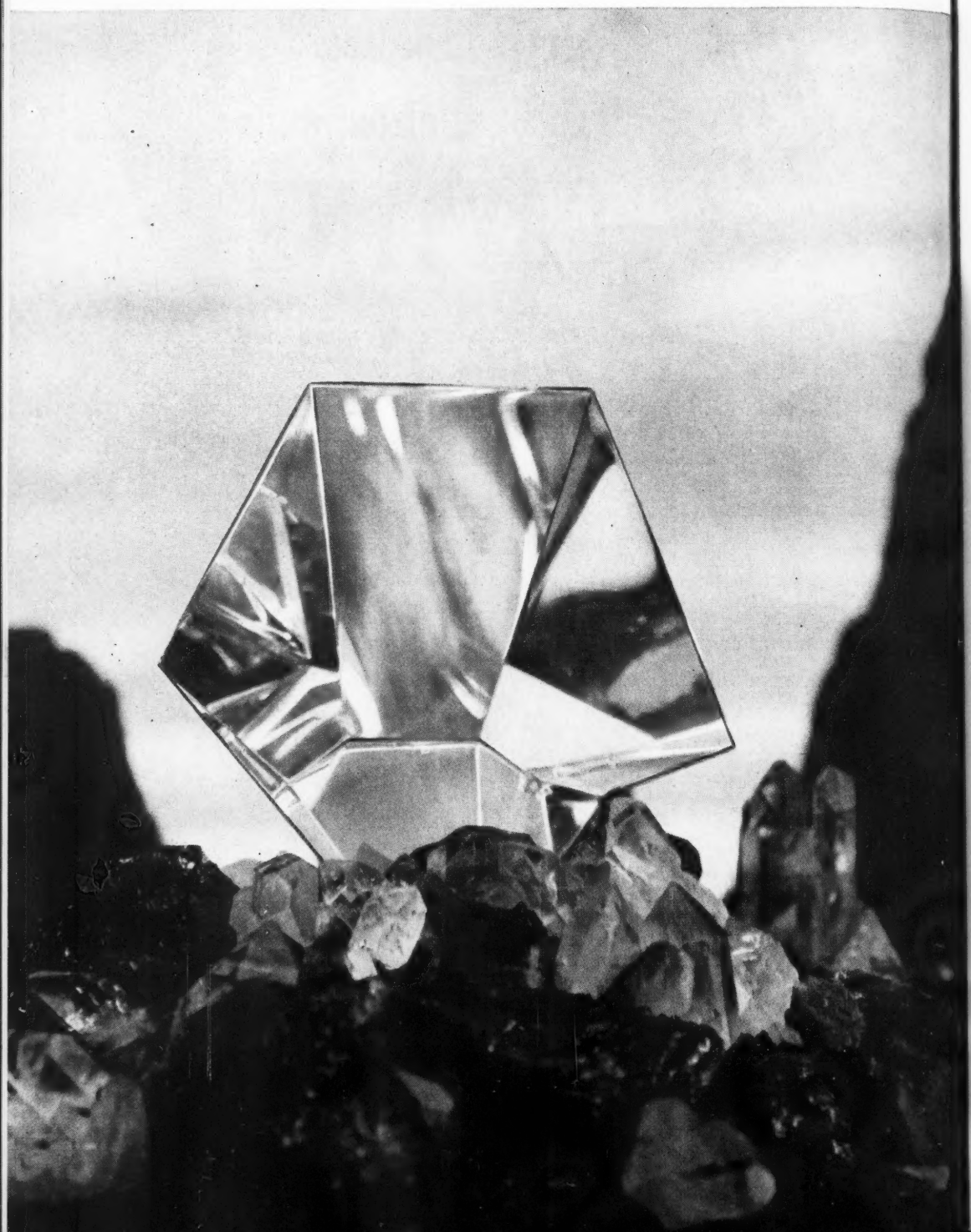
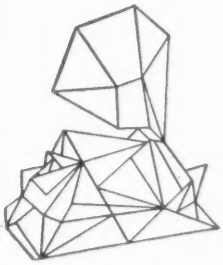
BECAUSE DĪSOMER SHEDS THE MOLECULAR DROSS



NEW...IN THE TREATMENT OF ALLERGIC DISORDERS



- *"...high therapeutic index"[1]*
- *unsurpassed clinical efficacy*
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- *side effects reduced to placebo level*

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2 mg. Tablet	q.i.d.
Syrup 1 teaspoonful	q.i.d.

**Chronotab* is White's repeat-action tablet.*

References: (1) Gould, A. H. and Long, D. L.: Clinical Pharmacology and Therapeutic Use of Dexbrompheniramine Maleate (Disomer), a new Histamine Antagonist (submitted for publication). (2) Medical Department, White Laboratories, Inc.

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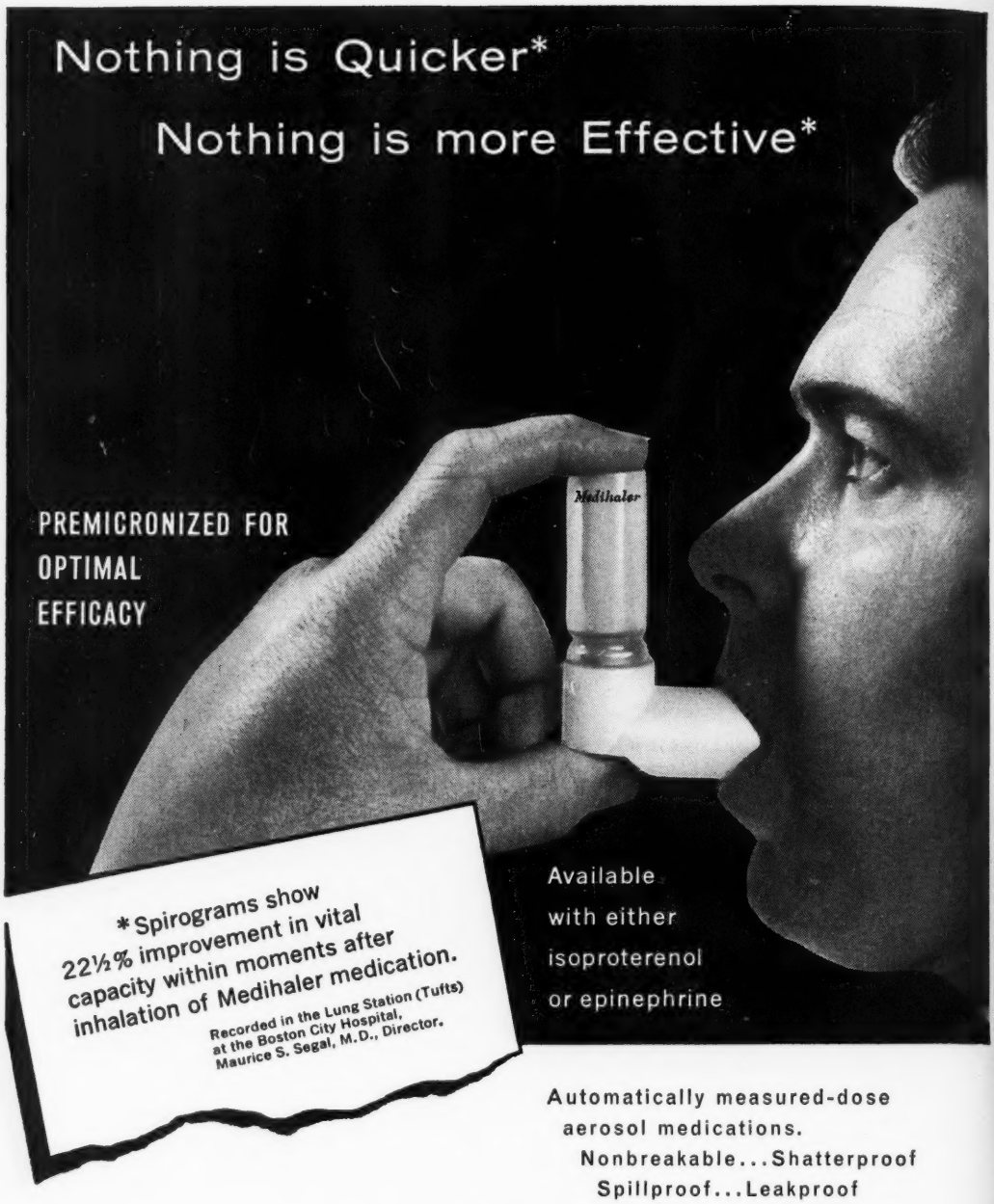
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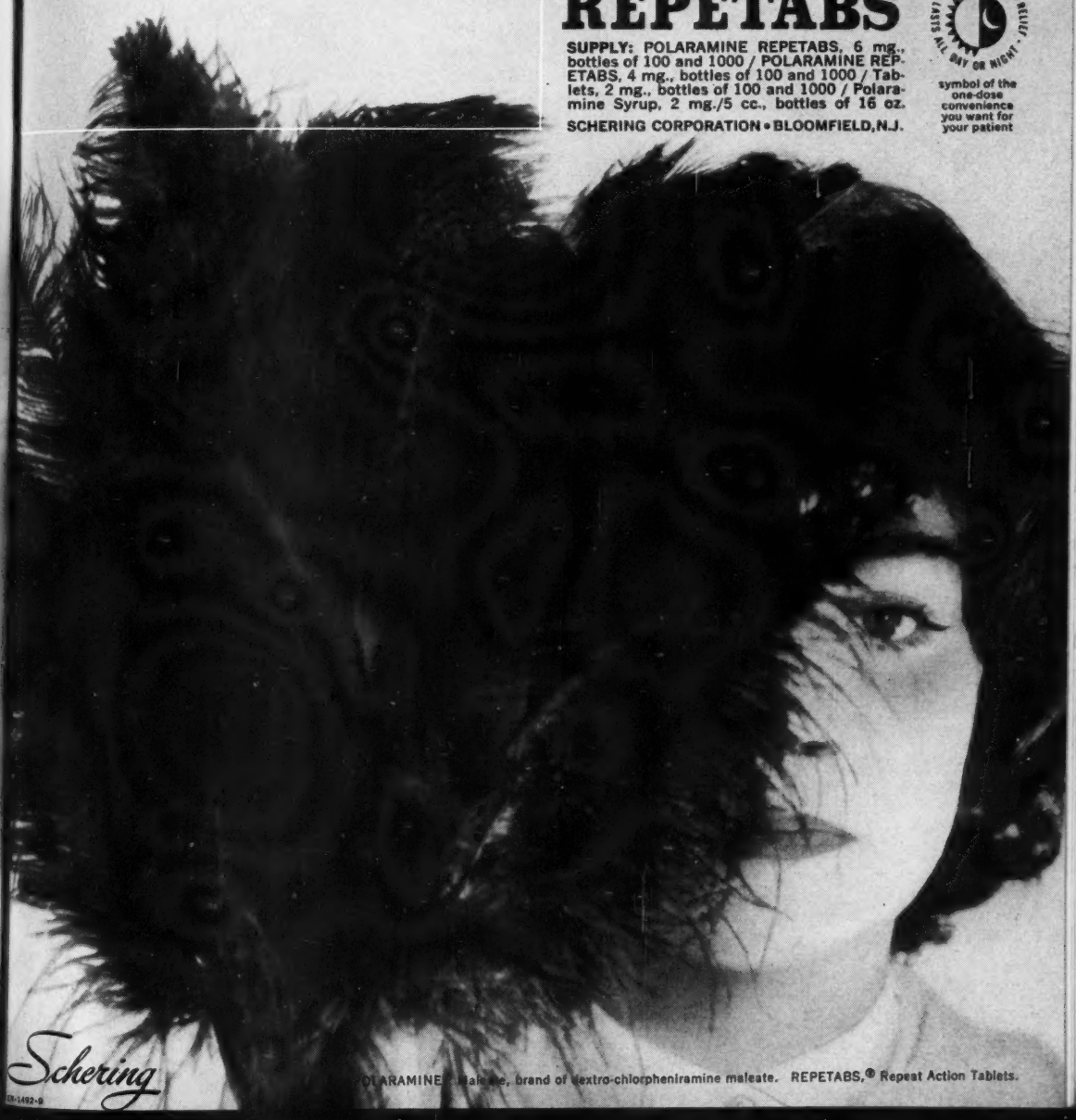

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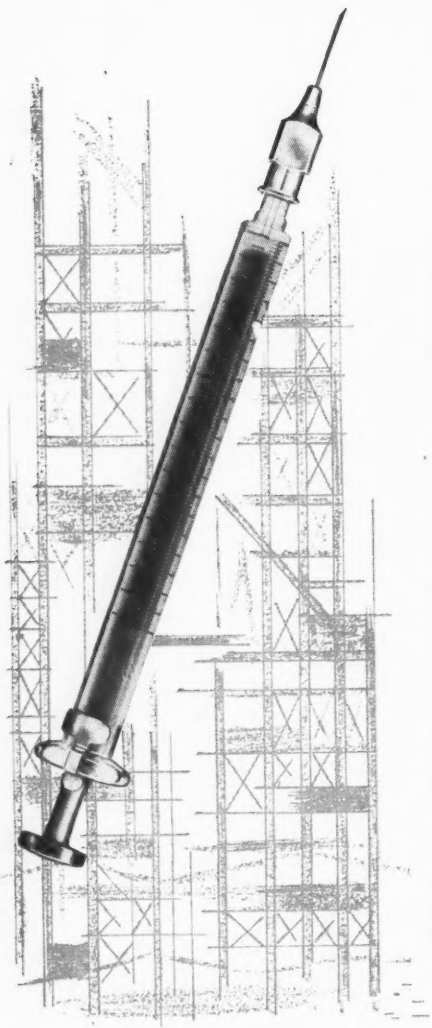

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proven by long clinical use.

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Levin, Samuel J.: Management of the Acute Asthmatic Attack in Childhood. Ped. Clin. of N. A. *1*:975, (November) 1954.

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Naterman, H. L.: Epinephrine Base Suspended in Water with Thioglycollate. J. Allergy *24*:60, (Jan.-Feb.) 1953.

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Unger, A. H., and Unger, L.: Prolonged Epinephrine Action. A Report on Use of an Epinephrine Suspension. Ann. Allergy *10*:128, (Mar.-Apr.) 1952.

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Jenkins, C. M.: A Clinical Study of "Sus-Phrine", an Aqueous Epinephrine Suspension for Sustained Action. J. Nat. M. A. *45*:120. (Mar.) 1953.

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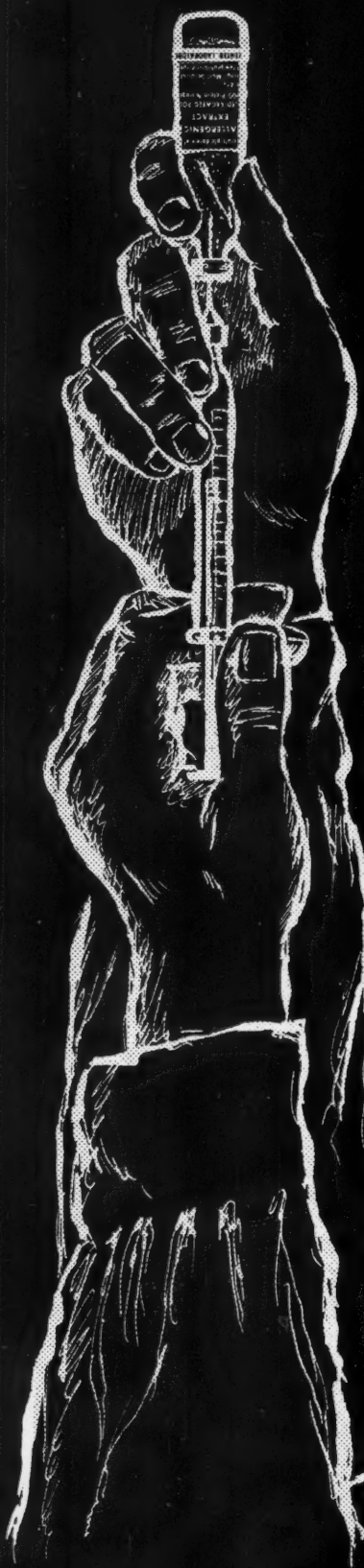

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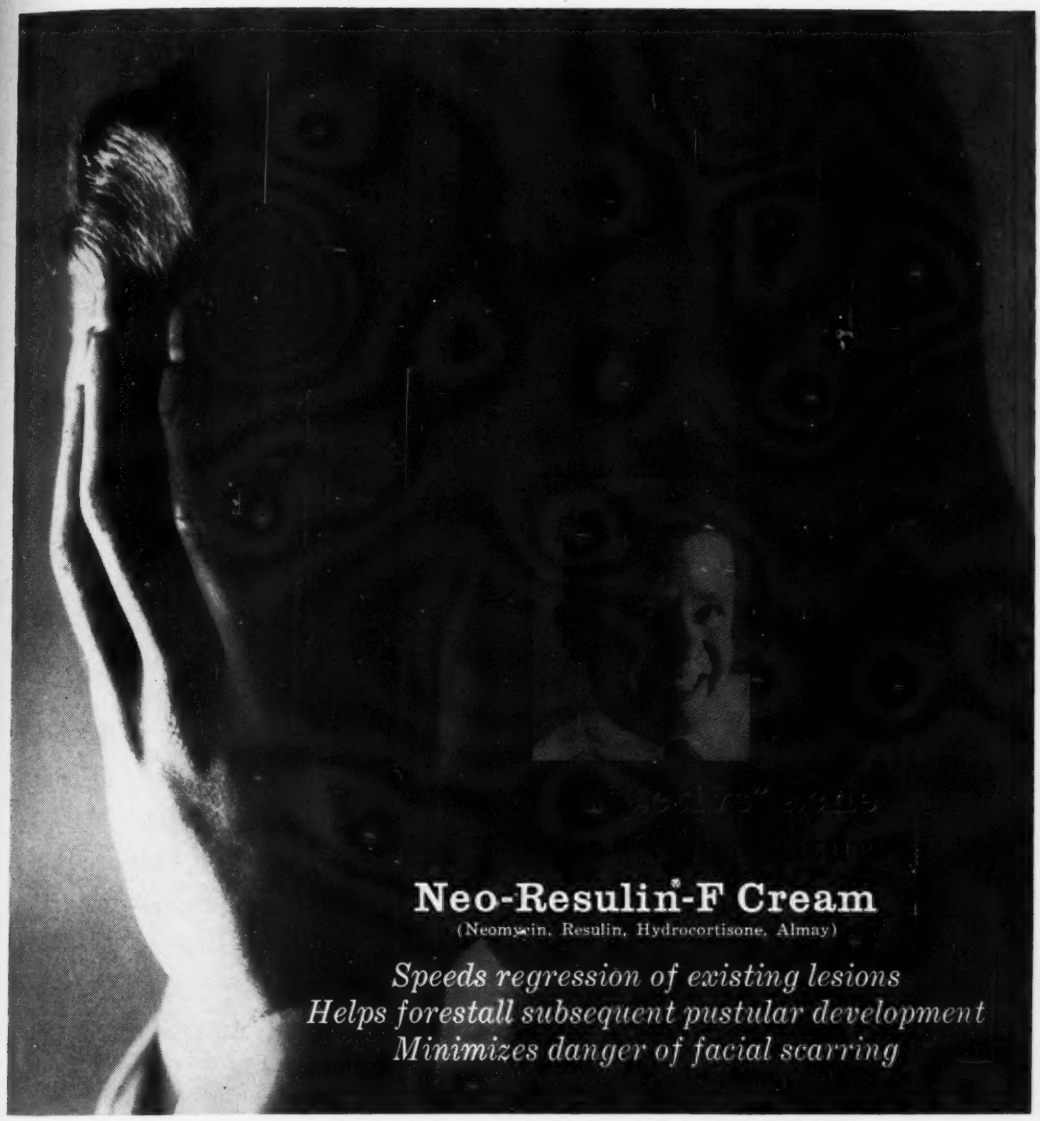
(1) Silbert, N. E., Ciba Clinical Symposia, 6: 86: May 1954
(2) Mechaneck, I., Annals of Allergy, 12: 164: March 1954
(3) Rosen, F. L., J. Med. Soc. N.J., 51: 110: March 1954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1. Schluger, J. et al.: Am. J. Med. Sci. 233:296, 1957.
2. Bradwell, E. K.: Acta med. scand. 146:123, 1953.
3. Truitt, E. B. et al.: J. Pharm. Exp. Ther. 100:309, 1950.

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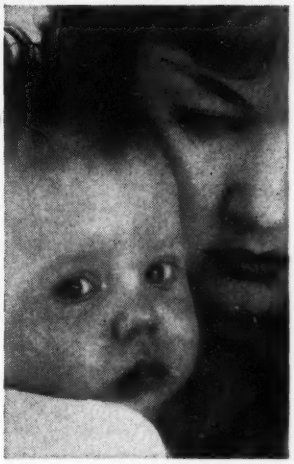

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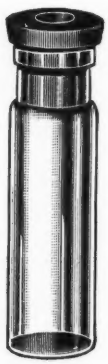

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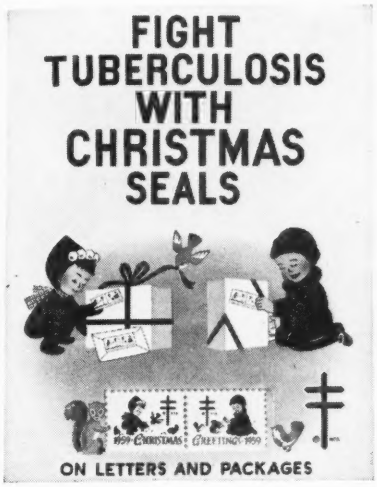

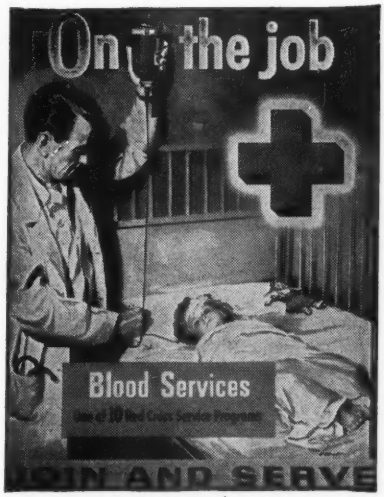

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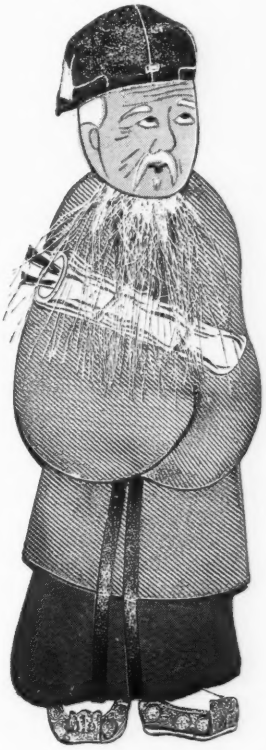

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Separatum Vol. 12, No. 1-5; Vol. 13, No.1-4; Vol. 14, No. 1-4; and Vol. 15, No. 1-3 INT. ARCH. ALLERGY

From the preface

When my fellow editors asked me to plan and edit the Béla Schick Festschrift, I decided that this volume should contain articles by leading medical scientists and physicians on topics in allergy and immunology in which they were most interested, and especially qualified to write about. The enthusiastic response that I had to my letters of invitation is but one measure of the universal respect and admiration which the scientific world has for Béla Schick. The papers in this volume represent only a small sampling of the world of allergy and immunology as it exists today. As in all samplings, not every possible subject has been included, but many important qualified to write about. The enthusiatic response that I had to my

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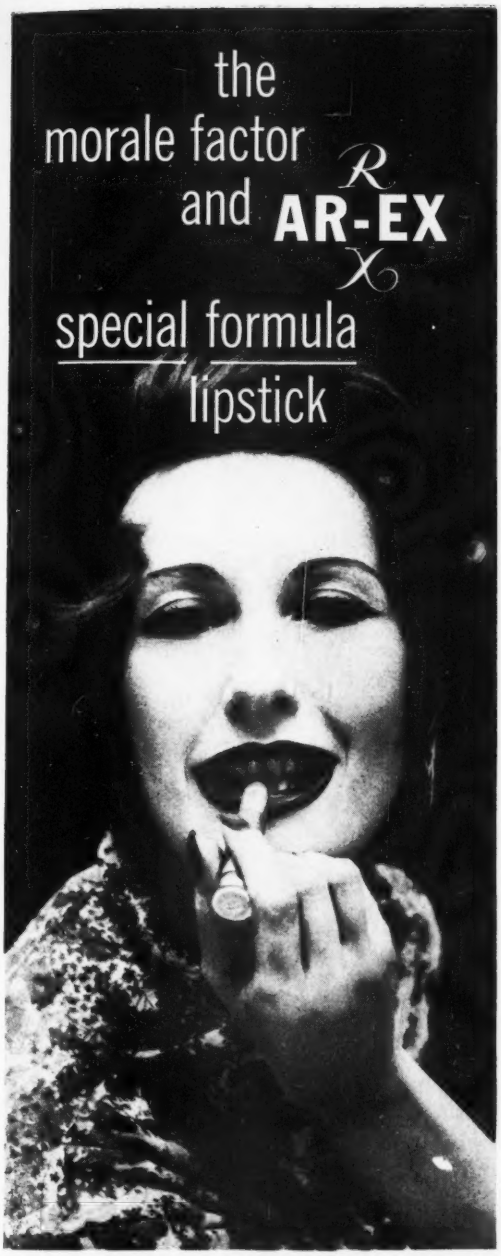

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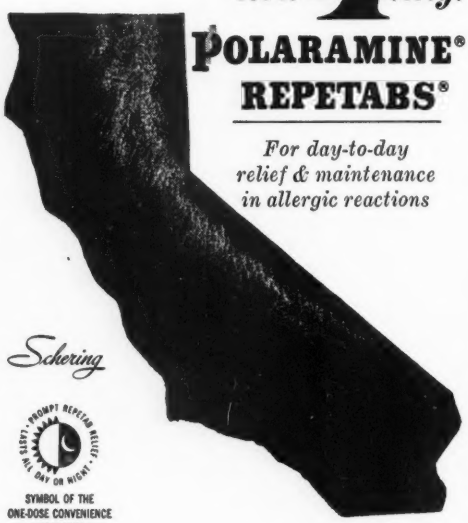

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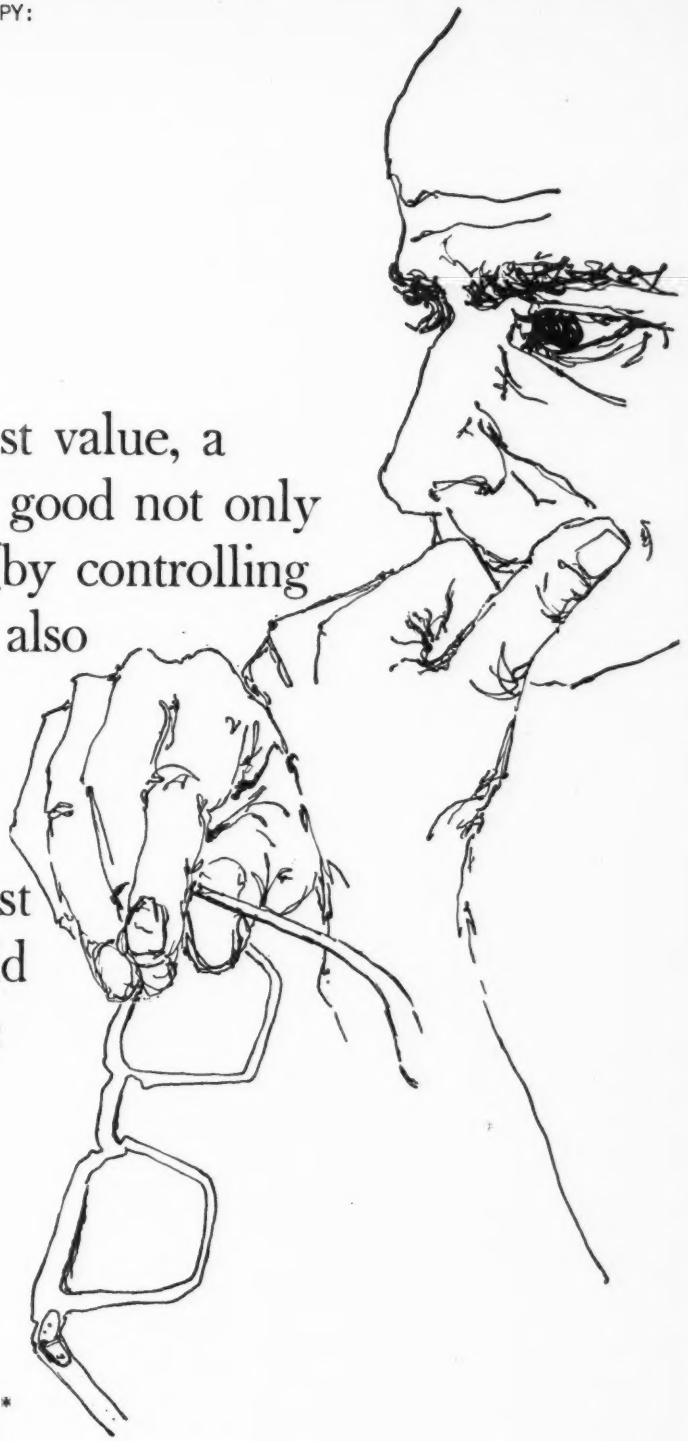

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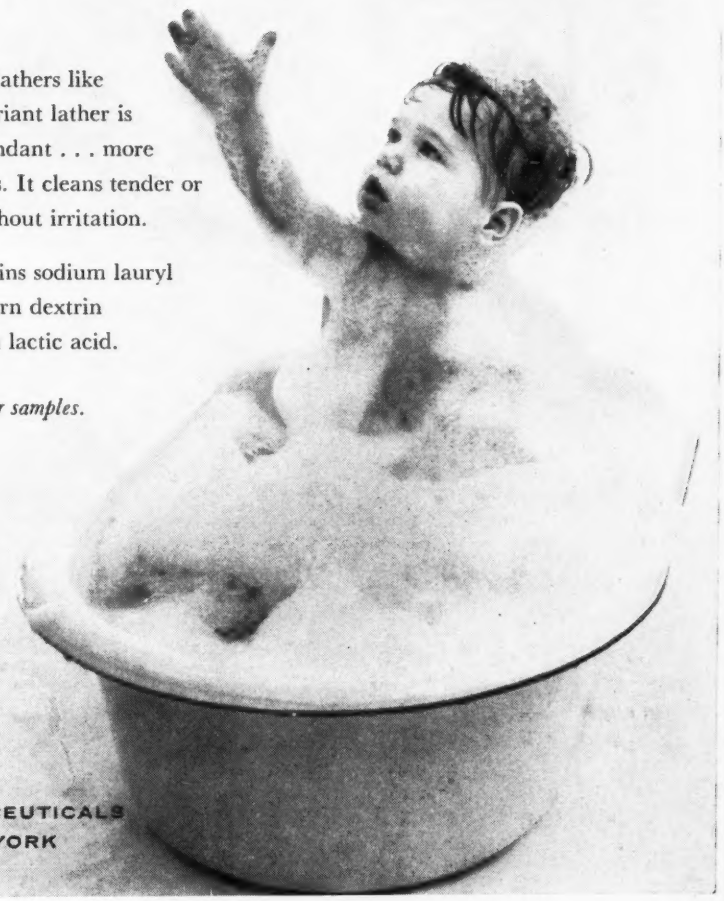

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